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August 8, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: **Docket No. FDA-2014-N-0189 (RIN 0910-AG38) (79 Fed. Reg. 23142) (April 25, 2014) – Comments on Proposed Rule "Deeming Tobacco Products to be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products"**

Altria Client Services Inc. ("ALCS"), on behalf of Nu Mark LLC ("Nu Mark"),[1] appreciates the opportunity to comment on the Food and Drug Administration's ("FDA" or "the Agency") Notice of Proposed Rulemaking ("Proposed Rule") on the deeming of tobacco products subject to the Food, Drug, and Cosmetic Act ("FDCA"), as amended by the Family Smoking Prevention and Tobacco Control Act ("FSPTCA").[2]

Altria, on behalf of its tobacco operating companies, supported the passage of the FSPTCA because it believed that a comprehensive regulatory framework, thoughtfully implemented, could contribute to resolving many of the complex issues that surround tobacco products. In exercising this authority, FDA should apply the FSPTCA based on science and evidence, recognizing differences between tobacco product categories, including noncombustible, tobacco-derived nicotine products ("TDNPs").

We continue to believe that reasonable regulation can benefit adult tobacco product consumers, including by providing a framework to evaluate tobacco products that are potentially less harmful than conventional cigarettes and by establishing clear principles for accurate and scientifically-grounded product-related communications. We thus support FDA extending its

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[1] Nu Mark is a wholly-owned subsidiary of Altria Group, Inc. ("Altria"). Green Smoke Inc. ("Green Smoke") is a wholly-owned subsidiary of Nu Mark. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout to refer to Nu Mark, except where the context requires otherwise.

[2] 79 Fed. Reg. 23142 (Apr. 25, 2014).

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regulatory authority over all tobacco products, including those containing tobacco-derived nicotine.

If you have questions, please contact me at (804) 335-2679.

Sincerely,

James E. Dillard III

Attachment

Comments on Proposed Rule

"Deeming Tobacco Products to be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products"

Submitted by
Altria Client Services Inc. on behalf of
Nu Mark LLC for the
Food and Drug Administration

August 8, 2014

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ALCS	Altria Client Services Inc.
APA	Administrative Procedure Act
ATC	adult tobacco consumer
CORESTA	Cooperation Centre for Scientific Research Relative to Tobacco
CPD	cigarettes per day
CPSA	Consumer Product Safety Act
CPSC	Consumer Product Safety Commission
CRO	contract research organization
EAIV	electronic age and identity verification
FCLAA	Federal Cigarette Labeling and Advertising Act
FDA	Food and Drug Administration
GRAS	generally recognized as safe
HPHC	harmful and potentially harmful constituent
ICH	International Conference on Harmonization
NIH	National Institutes of Health
NRT	Nicotine Replacement Therapy
NYTS	National Youth Tobacco Surveys
OTC	over-the-counter
PMTA	premarket tobacco product application
SE	substantial equivalence
TDNP	tobacco-derived nicotine product
USP	U.S. Pharmacopeia

Executive Summary

By extending its authority to all tobacco products, including e-vapor products, FDA will for the first time bring all tobacco products under a single public health regulatory authority. Altria's tobacco operating companies, including Nu Mark, have consistently urged FDA to implement a regulatory framework, grounded in science and evidence, that recognizes the differences in tobacco products, respects adult consumers' right to make informed choices, and fosters innovation in tobacco products.

The combination of new, innovative, and potentially less harmful tobacco products and adult tobacco consumer ("ATC") interest in them presents FDA with an unprecedented opportunity to reduce the harm associated with tobacco use. Flexible and thoughtfully tailored regulation can spur innovation in e-vapor and other novel, noncombustible tobacco products.

Our Comments to the Proposed Rule address numerous topics. In this Executive Summary we highlight several of these topics:

A. FDA's regulatory framework should recognize the harm reduction continuum and the role that TDNPs may play in reducing the population harm associated with the use of tobacco products

Effective science- and evidence-based regulatory approaches that recognize that different categories of tobacco products present different risks could provide a platform to develop, assess, and commercialize products that reduce the risk and harm from cigarette smoking. FDA's regulations should encourage and support manufacturers' efforts to develop new, potentially less harmful products, including e-vapor and other TDNPs. Impeding innovation that may reduce health risks could preserve cigarette smoking as the dominant form of tobacco use in the United States, an outcome FDA has described as unacceptable.

Although the e-vapor category is still relatively new, some public health and tobacco control researchers have reached the preliminary conclusion that e-vapor products may present a compelling risk reduction opportunity. E-vapor products likely pose a far lower risk to individual consumers than the risk posed by combustible tobacco products. In addition, e-vapor products have the potential to reduce the population harm associated with tobacco use. While important research needs remain, early evidence suggests that e-vapor products are used primarily by ATCs seeking an alternative to conventional cigarettes and that use of e-vapor products may facilitate complete switching from smoking.

While the available science is encouraging, we agree that FDA should strengthen the science and evidence base for e-vapor and other innovative tobacco products that have the potential to reduce individual risk and population harm.

B. FDA should establish product pathways that are consistent with Congressional intent, encourage innovation of potentially reduced harm products and provide a feasible path to market for such products

We urge FDA to implement product pathways that reflect reasonable regulation, comply with the requirements of the FSPTCA, conform with Congressional intent, and support manufacturers' efforts to develop and bring to market innovative, potentially reduced risk products.

FDA can achieve these goals in a number of ways. For example, FDA should exercise its statutory authority and discretion to establish an alternative grandfather date for deemed tobacco products. A logical date would be the effective date of the Final Rule. This would make the substantial equivalence ("SE") pathway a viable option for potentially reduced risk products that are already on the market and for which the SE pathway was specifically designed.

Nothing in the FSPTCA requires FDA to engage in all-or-nothing deeming for all purposes. Rather than deem an entire class of tobacco products categorically subject to the FSPTCA for all purposes, FDA has multiple options for proceeding in a reasoned, scientifically sound, and incremental manner. For example, FDA should exercise its statutory authority to deem e-vapor products commercially marketed before the Final Rule for certain purposes under the FSPTCA. Such products would be subject to age-restrictions, warning labels, and disclosure requirements, without subjecting them to premarket authorization. Only those e-vapor products commercially marketed after issuance of the Final Rule would be subject to all aspects of the FSPTCA, including premarket authorization.

Alternatively, FDA should deem e-vapor and other TDNPs, regardless of when they enter the U.S. market, subject to certain sections of the FSPTCA but not the premarket authorization requirements. FDA could achieve its public health objectives by subjecting these products to FSPTCA provisions governing the manufacture, labeling, and sale of the products. This approach would also allow FDA to monitor products and address compliance issues through post-market enforcement. FDA has adopted a similar approach for a variety of consumer products such as dietary supplements and certain over-the-counter drugs. The European Union has also adopted a similar framework for e-vapor products and there is no reason why this regulatory strategy could not work here.

FDA should also implement accelerated or modified premarket tobacco product application ("PMTA") pathways for deemed products. Specifically, FDA should consider creating an accelerated review process and/or a product and performance standards process for newly regulated and future products. In the past, FDA has similarly used its statutory authority and discretion to develop flexible approval policies, modified processes, and non-enforcement policies for certain classes of drugs, medical devices, and other products. Consistent with these approaches, FDA should employ such strategies to foster important health goals, avoid impractical outcomes, encourage innovation of new products, and promote fairness and efficiency in deemed tobacco product categories that are potentially less harmful.

C. Established definitions for components, parts, accessories, and other key terms are critical for FDA to effectively administer the deeming regulations

To effectively administer the deeming regulations, FDA should establish definitions for components, parts, accessories, and other terms that reflect a risk-based approach. For example, FDA's definitions should consider the relative risks posed by various types of components and parts under specific conditions of use and impose the least burdensome requirements necessary to effectively manage or mitigate those risks. This approach would be consistent with sound risk-based principles for the regulation of other products sold or distributed to consumers. These regulatory definitions should be flexible enough to encompass each category of deemed tobacco products, as well as different regulatory requirements that may apply to components and parts within a particular product category and specific enough to allow both FDA and industry to readily distinguish regulated items from unregulated items.

D. FDA's proposed warning for e-vapor and other TDNPs products is appropriate

FDA has proposed the following: "WARNING: This product contains nicotine derived from tobacco. Nicotine is an addictive chemical" for all tobacco products that it does not currently regulate, including e-vapor products.

We agree that the content of the proposed addiction warning is appropriate for e-vapor and other TDNPs.

FDA should, however, reduce the warning size for deemed tobacco products that carry only the addiction warning. For such products, the proposed warning can be clearly and conspicuously communicated to consumers without occupying 30 percent of both principal packaging display panels and 20 percent of advertising space. Requiring warnings larger than necessary to convey the addiction message to consumers would be inconsistent with the First Amendment.

E. Nu Mark supports FDA's proposal to establish a federal minimum age to purchase tobacco products

We support FDA's proposal to establish a minimum age of 18 to purchase tobacco products, including e-vapor products. Kids should not smoke or use any other tobacco product.

F. Tobacco product manufacturers should not use children's cartoons or youth-oriented candy trademarks to market their products

Many have expressed anger and frustration at certain tobacco product manufacturers using children's cartoon characters and youth-oriented candy trademarks to market their products. We share this concern. No tobacco product manufacturer should use names like Poppa Smurf, Curious George, Sweet Tarts, and Skittles to market their tobacco products. We believe addressing such activities should be part of FDA's initial focus as it regulates deemed tobacco products.

If and when FDA takes action to regulate deemed tobacco products with characterizing flavors, it must follow the process established in Section 907. This approach would ensure that any proposed regulatory action is supported by science and evidence, that the public is provided with notice and an adequate opportunity to comment, and that any standard is uniformly applied to all regulated entities. FDA should also take adult consumer preferences into account and consider the positive role that flavors may play in harm reduction.

Section I. Nu Mark and E-Vapor Category Overview

A. Background on Nu Mark

Nu Mark is an Altria company focused on responsibly developing and marketing innovative tobacco products for ATCs.

Nu Mark markets MarkTen® e-vapor products,[3] which contain tobacco-derived nicotine. Nu Mark currently distributes rechargeable MarkTen® e-vapor products in Indiana and Arizona and began the national expansion of MarkTen® e-vapor products in June in the Western half of the U.S.

In April 2014, Nu Mark acquired the e-vapor business of Green Smoke, Inc. and its affiliates. Green Smoke currently markets its e-vapor products under the GreenSmoke® brand in both rechargeable and disposable forms.

MarkTen® and GreenSmoke® e-vapor products use cartridges, which are closed-container systems. Nu Mark and GreenSmoke e-vapor cartridges are sold pre-filled and are not designed to be opened or refilled. Rather, the cartridges are intended to be discarded properly after use, thus reducing the risk of contact with liquid nicotine.

Both companies sell charging devices for their rechargeable products. Today, MarkTen® e-vapor products are sold at retail. In addition, items such as chargers are available for purchase at retail and online through an age-verified system. GreenSmoke® products are presently available online through an age-verified system and limited distribution at retail.

Nu Mark also currently markets VERVE® discs in Virginia. VERVE® discs are TDNPs designed to appeal to adult smokers interested in innovative oral tobacco product alternatives to cigarettes. Each disc contains tobacco-derived nicotine, non-tobacco cellulose fibers, flavorings, and a polymer. ATCs put the product in their mouth and chew on it, discarding it when done.

B. E-vapor category overview

An e-vapor tobacco product is a battery-powered tobacco product that allows consumers to inhale a heated vapor. The basic components are a power source, a heating element or "atomizer," and a liquid reservoir. E-vapor products typically contain a liquid solution of nicotine (usually derived from tobacco), propylene glycol, glycerin, flavors, and water.[4]

A consumer draws on the product mouthpiece to activate the atomizer's heating element. The atomizer heats the liquid, creating a vapor that the consumer can inhale.[5] Because e-vapor

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[3] Nu Mark uses the term "e-vapor products" when discussing products available in the e-vapor category. Here, when addressing third party studies, publications or surveys, we use the term used by the author of that study, publication or survey (*e.g.*, e-cigarettes).

[4] Orr (2014); Cahn & Siegel (2011); Caponnetto *et al.* (2013a). *See* Appendix A (a reference list of each scientific publication cited in these Comments).

[5] FDA Consumer Update, E-cigarettes: Questions and Answers, *available at* http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm225210.htm.

products do not burn tobacco, they do not produce smoke. Rather, consumers inhale and exhale a vapor,[6] an action that consumers often describe as "vaping."[7]

There are numerous e-vapor products on the market today, including disposable and reusable forms, non-refillable closed cartridge systems, refillable tank systems, liquid solutions comprising different flavors and nicotine concentrations in both cartridges and bottles (sometimes referred to as "e-liquid" or "e-juice"), and various platforms to charge reusable e-vapor products.

While e-vapor products currently represent a small portion of total tobacco product category sales, interest and awareness among ATCs has driven category growth. We estimate that 90% of adult smokers are aware of e-vapor products and about two thirds have tried them. Only a small number of adult smokers report using e-vapor products daily.

E-vapor products are sold online, at convenience stores, so-called "vape shops," and tobacco retail stores. Internet sales initially made up the majority of sales, but today, retail and "vape shops" are the primary trade channels.

Section II. FDA's Adherence to Guiding Principles and Fundamental Legal Requirements Will Help Ensure Successful Implementation of the Deeming Regulation

The following guiding principles are essential to effectively regulate deemed tobacco products, and we urge FDA to consider them as it develops its Final Rule.

A. Regulation should encourage innovation and establish flexible pathways to market for tobacco products that may benefit public health

By extending its authority to all tobacco products, FDA will for the first time bring all tobacco products under a single public health regulatory authority.[8] Altria's tobacco operating companies have consistently urged FDA to implement a regulatory framework, grounded in science and evidence, that recognizes the differences in tobacco products and fosters innovation that may benefit public health.[9]

FDA's leaders have articulated a compelling vision for the role of innovation in achieving FDA's public health objectives: "Innovation is also about finding new and better ways to do things to meet the needs and challenges before us."[10] The preamble to the Proposed Rule reflects this

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[6] Riker *et al.* (2012).

[7] Some researchers and international regulators refer to these products as electronic nicotine delivery systems ("ENDS").

[8] This would occur if FDA adopts "Option 1." "Option 2" would exempt so called "premium cigars" from regulation.

[9] *See* PM USA and USSTC, "Request for Comments: Regulation of Tobacco Products Under the Family Smoking Prevention and Control Act," Docket No. FDA-2009-N-0294 (Dec. 22, 2009) ("December 22, 2009, Regulatory Framework for Harm Reduction").

[10] Margaret A. Hamburg, "Remarks given at the NEHI Conference on Bridging the Innovation Gap" (April 26, 2012), *available at* http://www.fda.gov/NewsEvents/Speeches/ucm302037.htm.

vision. First, it recognizes the potential for regulation to "spur innovation" for tobacco products that have the potential to reduce harm.[11] Second, it acknowledges "the existence of a continuum of nicotine-delivering products that pose differing levels of risk to the individual."[12] Third, it seeks comments, research, facts, and other evidence about how to regulate tobacco products based on the continuum of risk.[13]

Flexible and thoughtfully tailored regulation can spur innovation in e-vapor and other novel, noncombustible tobacco products. Rigid and mechanistically applied regulation, by contrast, will thwart innovation – particularly if it prevents or unduly burdens new product introduction or the continued marketing of current products. Impeding innovation that may reduce health risks could also preserve cigarette smoking as the dominant form of tobacco use in the United States. FDA has described that outcome as unacceptable: "[m]aintaining the status quo and ensuring that things don't get any worse is not an acceptable solution."[14]

The potential for e-vapor products to transform the status quo is already evident. The e-vapor industry has experienced rapid growth since April 2011, when FDA first announced its intention to regulate these products as tobacco products. Consumer spending on e-vapor products in the United States is reported to have grown from less than $200 million in 2011 to approximately $1 billion in 2013.[15]

B. Regulation must be based on science and evidence

FDA's regulations and decision-making must be science- and evidence-based. Commitment to this standard protects the integrity of the Agency's decision-making process and provides a consistent and predictable regulatory environment for manufacturers. FDA leaders have stressed that science and evidence are central to making decisions about regulatory policy: "We need evidence to support any policy that we might enact, because it carries the force of law. When we are exploring our regulatory policy options, we focus on those that have the strongest support in the science base."[16]

Under FDA's leadership, many important research efforts are underway which will help guide future tobacco regulatory and policy decisions. These efforts include collaborating with the National Institutes of Health ("NIH") to conduct the first-of-its kind longitudinal study of the behavioral and health impact of tobacco and tobacco regulation,[17] establishing Tobacco Centers

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[11] 79 Fed. Reg. at 23149.

[12] 79 Fed. Reg. at 23147.

[13] *See* 79 Fed. Reg. at 23152, 23176-77.

[14] Ashley & Backinger (2012).

[15] *See* Alan Farnham. "E-Cigarette Sales to Hit $1 Billion." ABC News (Jul. 31, 2013), http://abcnews.go.com/Business/electronic-cigarette-sales-billion/story?id=19815486.

[16] Q&A: Mitchell Zeller on the FDA and Tobacco. (2014). *Cancer Discovery* 4: 10-11.

[17] The Population Assessment of Tobacco and Health (PATH) Study is a large-scale, national study of tobacco use. The initiative is the first large research effort by the NIH and FDA since Congress gave FDA authority to regulate tobacco products in the FSPTCA of 2009. The PATH study will follow more than 40,000 tobacco product users and those believed to be at risk for tobacco use. *See generally* FDA, "FDA and NIH announce joint study on tobacco use and risk perceptions," Press Release (Oct. 6, 2011), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm274626.htm; PATH, Population Assessment of Tobacco and Health, https://pathstudyinfo.nih.gov/.

of Regulatory Science to build expertise and to provide scientific evidence and information to inform regulation.[18] FDA also sponsors scientific workshops to encourage stakeholders to share information and perspective on important topics such as tobacco product analysis and modified risk tobacco products.[19]

As FDA assumes regulatory authority over new tobacco product categories, we encourage the Agency to continue its important research efforts. Robust scientific evidence and information will be the foundation for successfully developing and implementing a regulatory framework for deemed products. FDA has stated that it "do[es] not currently have sufficient data about e-cigarettes to determine what effect they have on the public health,"[20] and that "the health consequences of e-cigarettes are not well understood."[21] Although the available science is encouraging, we agree that FDA should strengthen the science and evidence base for e-vapor and other innovative tobacco products that have the potential to reduce individual risk and population harm.

C. Regulation should preserve and respect the choices of ATCs

Congress intended for FDA to respect ATC choice, while granting FDA authority to regulate tobacco products. In doing so, Congress explicitly preserved tobacco products as those that adults may use. A stated purpose of the FSPTCA was "to continue to permit the sale of tobacco products to adults in conjunction with measures to ensure that they are not sold or accessible to underage purchasers."[22] Congress also wanted ATCs to have the ability to choose a less harmful tobacco product, subject to effective FDA oversight.[23]

Congress gave FDA a powerful array of tools to reduce harm without depriving ATCs of choice. As FDA develops its Final Rule, we urge FDA to effectively use these tools and avoid onerous regulation that could deprive ATCs of choice.

D. ATCs are entitled to receive accurate, non-misleading information about tobacco products, including information about relative risk and harm reduction

Public health strategies to reduce tobacco-related disease should empower ATCs to make their own informed decisions. FDA can accomplish this by ensuring that ATCs receive information about tobacco products that may reduce their risk of disease compared to other tobacco products. The Strategic Dialogue recognized this principle, recommending that "[c]onsumers should be

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[18] *See* FDA, Tobacco Centers of Regulatory Science (TCORS), http://www.fda.gov/TobaccoProducts/PublicHealthScienceResearch/ucm369005.htm.

[19] *See* FDA, Tobacco Product Analysis - A Scientific Workshop (Jul. 30-31, 2013), http://www.fda.gov/TobaccoProducts/NewsEvents/ucm355041.htm; FDA, Public Workshop: Scientific Evaluation of Modified Risk Tobacco Product (MRTP) Applications (Aug. 25-26, 2011), http://www.fda.gov/TobaccoProducts/NewsEvents/ucm259201.htm.

[20] 79 Fed. Reg. at 23157.

[21] 79 Fed. Reg. at 23147.

[22] FSPTCA § 3(7).

[23] *See* FSPTCA § 3(4); § 911.

accurately informed and educated about relative risks of the use of different types of nicotine containing products."[24]

E. Regulation must not violate Constitutional principles

FDA's regulation must respect statutory and Constitutional limitations on its authority.[25]

Tobacco product labeling, advertising, and marketing are commercial speech protected by the First Amendment.[26] Four principles must guide FDA's approach to regulating deemed tobacco products: (1) FDA should focus on preventing underage tobacco use;[27] (2) small risks of underage exposure do not justify broad restrictions on communications with adult consumers;[28] (3) FDA has no legitimate interest in restricting the use of images, color, or sound in communications with adult customers;[29] and (4) FDA should consider the broader context and cumulative weight of regulations on tobacco companies' speech.

FDA must also ensure that its regulation does not constitute a "taking" in violation of the Fifth Amendment.[30] FDA must refrain from regulatory actions that arbitrarily or capriciously restrict manufacturers' ability to continue marketing their existing products or bring new products to market or unnecessarily reduce or eliminate the value of intellectual property (including trademarks) associated with those products.

F. Regulation should apply equally to all manufacturers

As a general principle, regulatory requirements should be the same for all manufacturers and importers. We believe the FSPTCA can benefit adult tobacco product consumers by establishing a common set of high standards for *all* manufacturers and importers doing business in the United States.

Consistent with that principle, FDA should not create special rules for small manufacturers and importers of deemed tobacco products by extending compliance periods or staggering compliance dates.[31] All manufacturers should comply with such fundamental requirements as

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[24] Zeller, *et al.* (2009) at 339.

[25] *See generally* PM USA and USSTC Comments on Docket No. FDA-2009-N-0294 (Regulation of Tobacco Products Under the Family Smoking Prevention and Tobacco Control Act (Dec. 22, 2009) ("Dec. 22, 2009 FSPTCA Comments"); PM USA Comments on Docket No. FDA-2010N-0568 (Required Warnings for Cigarette Packages and Advertisements) (Jan. 11, 2011).

[26] *See Lorillard Tobacco Co. v. Reilly,* 533 U.S. 525, 553-54 (2001) (tobacco advertising and marketing is protected commercial speech); *Discount Tobacco City & Lottery, Inc. v. United States*, 674 F.3d 509, 539 (6th Cir. 2012) ("[a]dvertising, marketing, and promotion of tobacco products" are protected "commercial expression").

[27] *See* December 22, 2009, FSPTCA Comments at 7-8 (Regulatory Framework for Harm Reduction).

[28] *See id.* at 8. *See also, e.g., Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 374 (2002) ("We have previously rejected the notion that the Government has an interest in preventing the dissemination of truthful commercial information in order to prevent members of the public from making bad decisions with the information."); *44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 503 (1966) ("The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good.").

[29] *See* December 22, 2009, FSPTCA Comments at 8-9.

[30] U.S. Const. amend. V, cl. 4.

[31] *See* 79 Fed. Reg. at 23177.

disclosing the locations of their facilities, the products that they manufacture or import, or the ingredients that are added to their products.

If FDA creates special rules for certain manufacturers and importers based on their size, it should clearly explain its rationale for doing so, including why such special rules are permitted by the FSTPCA, appropriate for the protection of public health, and necessary. If, rather than creating special rules, FDA decides to allow manufacturers and importers to petition on a case-by-case basis for additional time to comply with certain requirements, FDA should establish clear criteria to govern its decisions and a transparent process for making them consistently.

Section III. FDA's Regulatory Framework Should Recognize the Harm Reduction Continuum

FDA's regulatory framework for deemed tobacco products should be grounded in science and evidence, recognize the differences between categories of tobacco products, respect ATCs' right to make informed choices, and foster innovation in tobacco products that may have the potential to reduce harm. Importantly, the preamble to the Proposed Rule notes that some have advanced views that noncombustible tobacco products may be less hazardous than combustible products, and FDA has requested comments about how such products should be regulated.[32]

Today there are approximately 60 million ATCs in the United States, according to government data.[33] While conventional forms of tobacco, such as cigarettes, cigars, and smokeless tobacco, remain the most common, ATCs increasingly show an interest in new products, such as e-vapor.

At the individual level, it is well established that noncombustible, conventional tobacco products are less risky than combustible tobacco products.[34] The Director of FDA's Center for Tobacco Products recently acknowledged this in testimony before the U.S. Senate's Committee on Health, Education, Labor and Pensions.[35]

FDA's regulatory regime for deemed tobacco products should take into account these differences and maximize the opportunity for harm reduction. The statute already codifies the concept of tailored regulation. In debating the FSPTCA, Congress considered different tobacco product categories individually and made decisions on the appropriate level of regulation for each. For example, Congress determined that sampling is permissible for smokeless tobacco with certain restrictions, but inappropriate for cigarettes. Congress decided to ban characterizing flavors for cigarettes (other than tobacco and menthol), but to permit such flavors for smokeless tobacco

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[32] *See* 79 Fed. Reg. at 23147 and 23152.

[33] According to the 2012 National Survey on Drug Use and Health (NSDUH), 67 million adults (18+) reporting using tobacco products in the past 30 days. (*See* http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/DetTabs/NSDUH-DetTabsSect2peTabs1to42-2012.htm#Tab2.21A).

[34] There is overwhelming scientific, medical, and public health consensus that moist smokeless tobacco products, including those widely available in the United States (snuff and snus), are substantially less hazardous than cigarettes. *See, e.g.*, Zeller, *et al.* (2009); Hatsukami *et al.* (2007); Institute of Medicine (2007) at 327 (cigarette smoking is "undoubtedly" more hazardous than smokeless ("noncombustible") tobacco).

[35] http://www.help.senate.gov/hearings/hearing/?id=a0a14829-5056-a032-526d-3bc1bfd96586; http://www.c-span.org/video/?319401-1/fda-regulation-ecigarettes.

products. Congress also decided that graphic warnings were appropriate for cigarettes, but placed no such requirement on smokeless tobacco. FDA should take that same measured risk-based approach when extending its regulatory authority to deemed tobacco products.

There is a growing consensus that health policies based solely on prevention and cessation are not sufficient in the real world. Millions of adults are likely to continue using tobacco products notwithstanding efforts by government, public health, and others to encourage them not to do so.[36] Public health authorities, such as the U.K. Royal College of Physicians, recognize that "even with full implementation of all recognized effective tobacco control policies it will take many years for a marked reduction in smoking prevalence, and in the morbidity and mortality that smoking causes, to be realized."[37] A tobacco harm reduction approach thus is needed to complement proven prevention and cessation strategies.

The harm-reduction approach focuses on reducing tobacco-related morbidity and mortality by providing accurate information about consumer-acceptable tobacco products proven to be lower on the risk continuum of tobacco products. This continuum can be represented as shown in Figure 1.

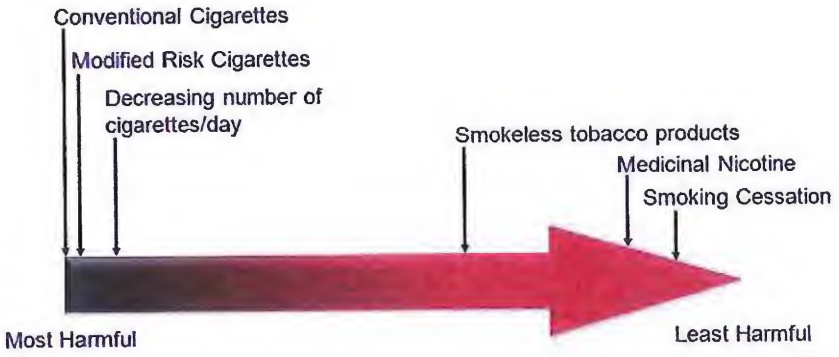

Figure 1. Risk continuum of tobacco products (directional only -- not to scale; adapted from Hatsukami *et al.* 2007)

Smoking conventional cigarettes is at one end of the continuum, presenting the highest health risk to the individual tobacco product consumer. Smoking cessation is at the opposite end.[38] Noncombustible tobacco products, such as smokeless tobacco products, are substantially lower on the risk continuum than cigarettes – closer, in fact, to medicinal nicotine and smoking cessation than to continued smoking.[39]

Effective science-and evidence-based regulatory approaches that recognize that different categories of tobacco products present different risks could provide a platform to develop, assess, and commercialize tobacco products that reduce the risk and harm from cigarette smoking.

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[36] Institute of Medicine (2007).

[37] United Kingdom Royal College of Physicians (2007) at 219.

[38] *See, e.g.,* Zeller *et al.* (2009); Hatsukami *et al.* (2007).

[39] Zeller *et al.* (2009) at 325.

Regulation should encourage and support manufacturers' efforts to develop new, potentially less harmful products. This approach would align with FDA's efforts to encourage innovation across all regulated products and should guide the future regulation of all tobacco products. Conversely, impeding innovation through burdensome regulation may maintain the status quo of cigarettes being the predominant form of tobacco use in the United States.

Section IV. TDNPs Have the Potential to Reduce the Population Harm Associated With the Use of Tobacco Products

TDNPs have the potential to reduce the harm associated with tobacco use. These products, which include e-vapor products like MarkTen® e-cigarettes and VERVE® discs are likely much lower on the risk continuum than are combustible tobacco products.

The combination of new, innovative, and potentially less harmful tobacco products and ATC interest in them presents FDA with an opportunity to reduce the harm associated with tobacco use because of the following:

- E-vapor products likely pose a far lower health risk to individual consumers than the risk posed by combustible tobacco products.
- E-cigarettes are primarily used by ATCs seeking an alternative to conventional cigarettes.
- Use of e-cigarettes is low among youth and largely limited to youth who report that they also use conventional tobacco products.
- Evidence suggests noncombustible tobacco products may facilitate complete switching from smoking.
- Evidence suggests adult smokers who use noncombustible tobacco products reduce their cigarette consumption, which may be a predictor of future complete switching from smoking.

Consistent with these findings, in July 2014, Hajek *et al.* reported the results of their review of available research. They found "preliminary evidence that [e-cigarette] use facilitates both quitting and reduction in cigarette consumption in smokers interested in quitting smoking and that "[r]egular use of [e-cigarettes] by non-smokers is rare and no migration from [e-cigarettes] to smoking has been documented (let alone whether this occurred in individuals not predisposed to smoking in the first place)."[40]

A. E-vapor products likely pose far lower risk to individual consumers than do combustible tobacco products

Although the e-vapor category is still relatively new, some public health and tobacco control researchers have reached the preliminary conclusion that e-vapor products may present a compelling risk reduction opportunity. For example, the Royal College of Physicians recently stated:

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[40] Hajeck *et al.* (2014).

> The main benefit of e-cigarettes, therefore, is that they provide inhalable nicotine in a formulation that mimics the behavioural components of smoking but has relatively little risk. And for the smoker who cannot quit, or wants to continue to use nicotine in a manner that resembles smoking, e-cigarettes are an obvious choice. Switching completely from tobacco to e-cigarettes achieves much the same in health terms as does quitting smoking and all nicotine use completely.[41]

E-vapor products likely have a lower risk profile than combustible cigarettes because the chemical composition of the vapor is much less complex than that of cigarette smoke.[42] In comparing levels of chemical constituents in e-cigarettes and conventional cigarettes, Goniewicz *et al.* concluded:

> The results of the study support the proposition that the vapour from e–cigarettes is less injurious than the smoke from cigarettes. Thus one would expect that if a person switched from conventional cigarettes to e-cigarettes the exposure to toxic chemicals and related adverse health effects would be reduced.[43]

A recent report commissioned by Public Health England reached a similar conclusion stating:

> [O]verall however the hazards associated with use of [e-cigarette] products currently on the market is likely to be extremely low, and certainly much lower than smoking.[44]

FDA's analyses of early versions of e-cigarette liquids and vapors indicated inconsistent nicotine content relative to labeling and the presence of low levels of some tobacco related chemicals.[45] More recent studies by Trehy *et al.* and Vansickel & Eissenberg have reported more consistent levels of nicotine in e-cigarette liquids[46] and more reliable nicotine deliveries in newer versions of e-cigarette products.[47] While trace levels of some tobacco related chemicals still exist in some e-cigarette liquids, the levels are much lower than regular cigarette smoke and similar to those in Nicotine Replacement Therapy ("NRT") products.[48] For all e-vapor products, however, the chemical composition of the inhaled aerosol will be impacted by the particular e-vapor liquid used and the device "component" used to aerosolize it. Important research needs remain as it relates to population effects, but clinical studies to date have reported that e-cigarettes are well tolerated and do not produce serious adverse events following use for up to 24 months.[49]

Following a recent review of the available scientific literature, Polosa *et al.* concluded:

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[41] http://www.rcplondon.ac.uk/commentary/what-you-need-know-about-electronic-cigarettes

[42] Nutt *et al.* (2014); Goniewicz *et al.* (2014).

[43] Goniewicz *et al.* (2014).

[44] Britton & Bogdanovica (2014); *see also* Polosa *et al.* (2013a).

[45] Westenberger (2009).

[46] Trehy *et al.* (2011).

[47] Vansickel & Eissenberg (2013).

[48] Cahn & Siegel (2010).

[49] Caponnetto *et al.* (2013a); Polosa *et al.* (2013b).

> E-cigs might be the most promising product for tobacco harm reduction to date. E-cigs deliver a nicotine vapor without the combustion products that are responsible for nearly all of smoking's damaging effects.[50]

A recent analysis by Nutt *et al.* estimated the relative harms of tobacco and nicotine-containing products, including e-cigarettes and oral nicotine-containing products.[51] Considering both harms to consumers and others, Nutt *et al.* estimated the harm of e-cigarettes and oral nicotine-containing products to be approximately 4% and approximately 2% as harmful as conventional cigarettes, respectively.

B. E-cigarettes are primarily used by ATCs seeking an alternative to conventional cigarettes

Based on surveys of e-cigarette consumers, Etter & Bullen and Goniewicz *et al.* reported that e-cigarette consumers use these products primarily to quit smoking, reduce regular cigarette consumption, or because they perceive them as a less harmful alternative to cigarettes.[52] Specifically, Etter & Bullen reported respondents' reasons for using e-cigarettes were as follows: to quit or reduce smoking (92%); belief that it was less toxic (84%); help with craving (79%) and withdrawal symptoms (67%); cheaper than conventional cigarettes (57%); and could help them deal with situations where they could not smoke (39%). Seventy-nine percent of these study participants who had quit smoking conventional cigarettes said they were concerned about relapse to cigarettes if they stopped using e-cigarettes.[53]

Among the U.S. adult population, current use of e-cigarettes is low, but increasing. McMillen *et al.* reported adult current e-cigarette use was 0.35% in 2010,[54] and Zhu *et al.* reported current adult e-cigarette use to be 1.44% in 2012.[55] Recently, the CDC reported 1.9% of U.S. adults use e-cigarettes "every day" or "some days" based on the 2012–2013 wave of the National Adult Tobacco Survey.[56]

Two nationally representative surveys evaluated current e-cigarette use among adults by age, gender, race/ethnicity, income, education and geographic region in 2010 and 2012. Regan *et al.* reported no major differences in rates of current e-cigarette use by gender, race/ethnicity, income, education or geographic region in 2010.[57] Of note, these authors found that adults who used multiple tobacco products were more likely to currently use e-cigarettes than adults who used only one tobacco product and that adults who used conventional tobacco products were more likely to currently use e-cigarettes than those who did not use conventional tobacco

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[50] Polosa *et al.* (2013a).

[51] Nutt *et al.* 2014.

[52] Etter & Bullen (2011); Goniewicz *et al.* (2013).

[53] Etter & Bullen (2011).

[54] McMillen *et al.* (2012) reported that the proportion of adults who had ever used e-cigarettes (1.8%) and the proportion of those who reported current use (19.7%). ALCS calculated overall prevalence based on these two proportions.

[55] Zhu *et al.* (2013).

[56] Centers for Disease Control and Prevention (2014).

[57] Regan *et al.* (2013).

products.[58] Zhu *et al.* reported that in 2012 rates of current e-cigarette use were not different by gender. Non-Hispanic Whites, however, were more likely to report current e-cigarette use than Hispanics and those of other races.[59]

Regan *et al.*, Pearson *et al.*, and Zhu *et al.* conducted nationally representative cross-sectional surveys measuring current e-cigarette use by smoking status. Table 1 summarizes prevalence of current e-cigarette use among current, former and never smokers from these studies.

Table 1. Current e-cigarette use among current, former and never smokers.[60]

Study author (year of publication)[61]	Survey month and year	Current e-cigarette use (%)		
		Current smokers	Former smokers	Never smokers
Regan (2013)	April–May 2010	3.12	0.89	0.62[62]
Pearson (2012)	June 2010	4.1	0.49	0.29
Zhu (2013)	February–March 2012	6.26	6.08	0.04

These data show that less than 1% of never cigarette smokers reported current e-cigarette use. Comparing survey data for 2010 and 2013, the largest increase in current e-cigarette use was among former smokers. Based on the cross-sectional design of these studies, there is insufficient information to determine directional changes in tobacco product use. It is, therefore, not clear whether these data indicate a relapse among former smokers from cigarette smoking cessation to e-cigarette use or whether e-cigarette use facilitated cigarette smoking cessation. Longitudinal studies or well-designed cross sectional surveys are needed to gain insight on these issues. The important point is that the available nationally representative data shows that e-cigarette use among U.S. adults is overwhelmingly confined to current and former smokers.

C. Use of e-cigarettes is low among youth and is largely limited to youth who report also using conventional tobacco products

Kids should not smoke or use any other tobacco product, including e-vapor products. As discussed in Section VIII, Nu Mark supports FDA's proposal to establish a minimum age of 18 to purchase deemed tobacco products. In the meantime, we have supported legislative and

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[58] *Id.*

[59] Zhu *et al.* (2013).

[60] Current e-cigarette use defined as past 30-day use in all referenced surveys. Current smoking defined as smoking some days or every day and smoking 100 cigarettes lifetime. Former smoking defined as currently smoking not at all and smoking 100 cigarettes lifetime. Never smoking defined as never having smoked 100 cigarettes lifetime.

[61] Regan *et al.* (2013); Pearson *et al.* (2012); Zhu *et al.* (2013).

[62] Publication provided data on the percent of current, former, and never smokers who had heard of e-cigarettes and the proportion of those who also reported past 30-day use of e-cigarettes. Data in the table were calculated from these two proportions. For example, 49.6% of current smokers reported awareness of e-cigarettes and 6.3% of these reported past 30-day use. Therefore, 6.3% of 49.6% yields 3.12% of current smokers who used cigarettes in the past 30 days.

regulatory efforts to restrict underage access to all tobacco products, including provisions requiring that all tobacco products at retail be sold in a non-self-service manner. To date, 39 states[63] have enacted underage access prevention laws. Nu Mark continues to support similar legislative efforts in the remaining states.

Data from the 2011 and 2012 National Youth Tobacco Surveys ("NYTS") provide the only publicly available nationally representative assessment of e-cigarette use among underage persons. Among high school students in 2011, 4.7% reported ever trying an e-cigarette. This percentage increased to 10.0% in 2012.[64] Prevalence of current e-cigarette use among high school students also increased from 1.5% in 2011 to 2.8% in 2012.[65]

These data provide little direct evidence, however, that high school students are initiating tobacco use with e-cigarettes. In 2011 and 2012, 92% and 90%, respectively, of high school students who had ever tried e-cigarettes also had tried at least two other tobacco products. Similarly, for both survey years, approximately 50% of high school students who reported ever trying an e-cigarette also reported past 30-day use of at least two other tobacco products. In 2012, only 2% of high school students who ever tried e-cigarettes reported never trying any tobacco product other than e-cigarettes.[66] In both 2011 and 2012, almost no high school students reported past 30-day use of e-cigarettes only.[67] Overall, these data suggest that high school students do not use e-cigarettes at high rates, and most of those who do, use multiple tobacco products. When analyzing this data it is important to note that 16% of NYTS respondents are 18 or older; therefore, estimates of prevalence among high school students include people of legal age to purchase tobacco products.

Some have posited that "e-cigarette use is aggravating rather than ameliorating the tobacco epidemic among youths."[68] Results of the 2011 and 2012 NYTS, however, show that while e-cigarette use increased as described, regular cigarette smoking declined during that same time period[69] (Figure 2). The data thus do not indicate that e-cigarette use has increased smoking prevalence among middle and high school students.

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[63] Alabama, Alaska, Arkansas, Arizona, California, Colorado, Connecticut, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Minnesota, Mississippi, Nebraska, Nevada, New Hampshire, New Jersey, New York, North Carolina, Ohio, Oklahoma, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

[64] Centers for Disease Control and Prevention (2013).

[65] Current use defined as past 30-day use.

[66] Based upon ALCS analysis of NYTS conducted on behalf of Altria's Underage Tobacco Prevention program. Proportion not calculated for 2011 due to fewer than 30 responses.

[67] Proportions not calculated due to fewer than 30 responses.

[68] Dutra & Glantz (2014).

[69] Centers for Disease Control and Prevention (2013).

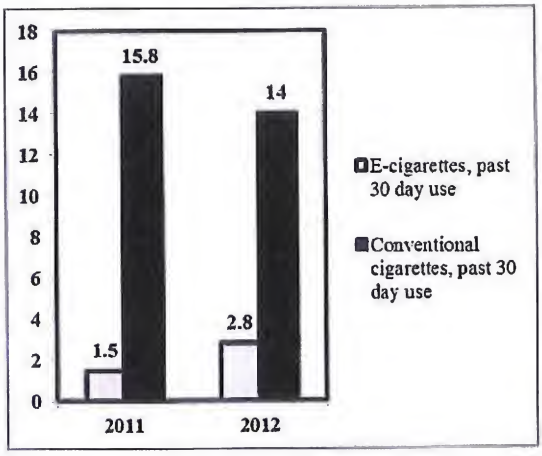

Figure 2. Past 30-day use of cigarettes and e-cigarettes among U.S. high school students (NYTS 2011 and 2012)

D. Evidence suggests e-cigarettes may facilitate complete switching from cigarette smoking

A majority of surveys of current e-cigarette consumers suggest that e-cigarettes may help cigarette smokers quit smoking. Etter and Goniewicz *et al.* reported the most common reason cigarette smokers cited for using e-cigarettes is to quit smoking conventional cigarettes.[70] Bullen *et al.* reported some smokers use e-cigarettes to reduce their desire to smoke,[71] and Pokhrel *et al.* reported smokers use e-cigarettes to help them achieve smoking cessation.[72]

Goniewicz *et al.* conducted an Internet survey of 179 e-cigarette consumers in Poland and reported that 64% of participants who smoked conventional cigarettes when they started using e-cigarettes had stopped smoking cigarettes at the time of the survey.[73] Almost all of the participants used e-cigarettes daily.

Foulds *et al.* surveyed 104 experienced e-cigarette consumers who, on average, had previously smoked 25 cigarettes per day ("CPD") and had tried to quit smoking nine times before they started using e-cigarettes.[74] Of these e-cigarette consumers, 78% had not used any other tobacco product in the 30 days prior to the survey. These results suggest use of e-cigarettes may have facilitated smoking cessation among this group of heavy cigarette smokers with a history of unsuccessful quit attempts.

Dawkins *et al.* conducted an on-line survey of 1,347 respondents from 33 countries; 74% of participants reported not smoking for at least a few weeks since using e-cigarettes.[75] Farsalinos *et al.* surveyed 111 ex-smokers who had switched completely from conventional to electronic

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[70] Etter (2010); Goniewicz *et al.* (2013).

[71] Bullen *et al.* (2010).

[72] Pokhrel *et al.* (2013).

[73] Goniewicz *et al.* (2013).

[74] Foulds *et al.* (2011).

[75] Dawkins *et al.* (2013).

cigarettes, 42% of whom reported quitting smoking during the first month of e-cigarette use.[76] While additional research needs remain, the overall results suggest that e-cigarettes help some consumers successfully quit smoking.

Etter & Bullen recently reported results of a longitudinal study tracking the smoking habits of 367 e-cigarette consumers for one year.[77] Only 6% of e-cigarette consumers who had quit smoking cigarettes relapsed and 46% reported quitting smoking after one year of follow-up.[78] Taken together, data from surveys of e-cigarette consumers show high levels of cigarette smoking cessation consistent with e-cigarette consumers' stated belief that e-cigarettes are effective in aiding cigarette smoking cessation.

Several clinical trials have reported that e-cigarette use resulted in modest rates of cigarette smoking cessation.[79] Follow up periods from these studies range from 1 to 24 months and cessation rates ranged from 7.3% to 46%. These cessation rates are generally comparable to rates reported in studies of NRT products.[80] Most of the studies included participants who said they were not interested in quitting smoking.[81] In a recent study, Brown *et al.* specifically evaluated 5,863 adult smokers who said they were interested in quitting and had made at least one quit attempt within the past 12 months.[82] The objective of the study was to assess the effectiveness of e-cigarettes when used to aid smoking cessation compared with nicotine replacement therapy and with unaided quitting. The investigators concluded:

> Among smokers who have attempted to stop without professional support, those who use e-cigarettes are more likely to report continued abstinence than those who used a licensed NRT product bought over-the-counter or no aid to cessation. This difference persists after adjusting for a range of smoker characteristics such as nicotine dependence.[83]

Not all studies, however, find evidence suggesting e-cigarette use may facilitate smoking cessation for some smokers. For example, Adkison *et al.*, Grana *et al.,* and Richardson *et al.* reported no apparent difference in quit rates between smokers using e-cigarettes and those not using e-cigarettes.[84] Dutra & Glantz, Lee *at al.*, and Vickerman *et al.* reported e-cigarette use was associated with lower odds of smoking cessation.[85] While cross sectional studies such as these are capable of identifying associations, they cannot determine causality or directionality. Thus, these studies cannot distinguish whether the use of e-cigarettes leads to cigarette smoking and failed quit attempts; or whether attempting and failing to quit leads smokers to use e-cigarettes.

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[76] Farsalinos *et al.* (2013).

[77] Etter & Bullen (2014).

[78] *Id.*

[79] Bullen *et al.* (2013); Caponnetto *et al.* (2013a; b); Etter & Bullen (2014); Polosa, *et al.* (2011; 2013b).

[80] Carpenter *et al.* (2013); Hughes *et al.* (2011).

[81] Bullen *et al.* (2013) included only smokers who stated interest in smoking cessation.

[82] Brown *et al.* (2014).

[83] *Id.*

[84] Adkison *et al.* (2013); Grana, *et al.* (2014); Richardson *et al.* (2014).

[85] Dutra & Glantz (2014); Lee *et al.* (2014); Vickerman, *et al.* (2013).

A word on NRT data seems appropriate: NRT product consumers are likely to smoke more cigarettes, be less successful at a quit attempt, and more likely to relapse than smokers using no cessation aid.[86] These outcomes are not caused by NRT itself; rather cigarette smokers who have difficulty quitting are more likely to use NRT products. Thus, it seems likely that failed quit attempts lead smokers to use e-cigarettes and not the other way around. It can be difficult to quit cigarette smoking, and many smokers who try to quit do not succeed. This should not deter someone from trying. Even among smokers intending to quit with the aid of NRT, quit rates average about 20%.[87] It stands to reason, therefore, that many smokers who have made failed quit attempts will have an interest in and use e-cigarettes.

E. Evidence suggests adult smokers who use e-cigarettes reduce their cigarette consumption, which may lead to future smoking cessation

While an encouraging body of evidence suggests e-cigarettes may help smokers quit, not all e-cigarette consumers quit smoking. However, several studies have reported that among e-cigarette consumers who continue to smoke, use of e-cigarettes leads to a substantial reduction in cigarettes smoked per day (Table 2).

Table 2. Reductions in cigarettes smoked per day (CPD) at baseline and follow up in longitudinal studies of e-cigarettes.

Study author (year of publication)[88]	Percent smoking reduction by follow up period (average baseline CPD – average follow up CPD)				
	1 week	1 month	6 months	12 months	24 months
Bullen (2013)	-	70% (18.4 - 5.5)	59% (18.4 - 7.6)	53% (18.4 - 8.7)	-
Caponnetto (2013a)	-	-	42% (19 -11)	37% (19 - 12)	-
Etter (2014)	-	47% (11.3 - 6.0)	-	-	-
Polosa (2011)	-	-	80% (25 - 5)	-	-
Polosa (2013b)	-	-	-	-	80% (25 - 4)
Polosa (2014)			91% (21.9 – 1.9)	92% (21.9 – 1.7)	
Wagener (2014)	44%	-	-	-	-

Overall, use of e-cigarettes appears to be associated with a substantial reduction in CPD within one month. For most study participants, cigarette smoking reductions appear to remain, on

[86] *See* Brown *et al.* (2014); Alpert *et al.* (2013).

[87] Carpenter *et al.* (2013); Hughes *et al.* (2011).

[88] Bullen *et al.* (2013); Caponnetto *et al.* (2013a); Etter and Bullen (2014); Polosa *et al.* (2011; 2013b; 2014); Wagener *et al.* (2014).

average, around 50% beyond one month. Investigators reported an overall reduction in CPD of 80% in the study with the longest follow-up period (24 months).[89]

In general, people smoking fewer cigarettes per day are more likely to quit smoking vs. people smoking more cigarettes per day.[90] Therefore, use of e-cigarettes among cigarette smokers which results in a reduction of CPD of conventional cigarettes may be a transitional phase leading to eventual smoking cessation.

Some have suggested that concurrent use of conventional cigarettes and e-cigarettes, referred to as dual use, results in little benefit for smoking related disease risk from reducing the number of cigarettes smoked per day.[91] However, such criticism fails to consider that even if dual consumers continue to smoke, by reducing their daily cigarette consumption, they may increase their likelihood of eventual smoking cessation relative to never using e-cigarettes. The percentage of current dual consumers of conventional cigarettes and e-cigarettes who will ultimately quit smoking remains unclear. FDA should commission longitudinal studies to better understand cigarette smoking quit rates among dual cigarette/e-cigarette consumers. FDA should also consider whether consumer communications might be appropriate to facilitate smoking cessation among the dual consumer population.

F. Oral TDNPs may play a significant role in harm reduction

Many adult cigarette smokers say that they are interested in trying new forms of noncombustible tobacco as alternatives to cigarettes. Oral TDNPs today represent a small part of total tobacco product sales, but over time could play a significant role in harm reduction. Like other noncombustible tobacco products, oral TDNPs are likely much lower on the continuum of risk than conventional tobacco products such as cigarettes.

One example of an oral tobacco-derived nicotine product is Nu Mark's VERVE® discs. VERVE® discs contain tobacco-derived nicotine, similar to that used in oral NRT products. Given that VERVE® discs are likely much lower on the continuum of risk compared with combustible tobacco products,[92] it is possible that products such as VERVE® could reduce the harm associated with tobacco use, especially as an alternative to cigarette smoking.

FDA regulation should support manufacturers' efforts to invest in these types of alternative products that may have the potential to reduce harm attributable to conventional tobacco products.

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[89] Polosa *et al.* (2013b).

[90] Breslau & Johnson (2000); Graham & Der (1999); Hyland *et al.* (2004); Hymowitz *et al.* (1997).

[91] Grana *et al.* (2014).

[92] Nutt *et al.* (2014).

Section V. Established Definitions for Components, Parts, Accessories and Other Key Terms are Critical for FDA to Effectively Administer the Deeming Regulation

The Proposed Rule would subject "components and parts" of deemed products to each FSPTCA requirement that currently applies to "tobacco products." "Components and parts" would, therefore, be subject to FSPTCA requirements related to labeling, registration and listing, submission of health information, new product premarket authorization pathways and warnings.[93] Components and parts that contain nicotine or tobacco would also be subject to the Proposed Rule's minimum purchase age and identification restrictions that apply to currently regulated tobacco products.

Neither the FSPTCA nor the Proposed Rule defines "components and parts", "accessory" or other important terms such as "finished tobacco product" or "consumption." FDA has requested comments on (1) whether it should define components and parts or accessory; (2) how its proposal to exclude accessories from deeming would impact public health;[94] and (3) how the use of certain components, parts, or accessories might be used to alter the effects of tobacco products on public health, the constituents delivered by the product, or the potential initiation of new tobacco consumers.[95]

Our comments address the following issues raised by the Proposed Rule:

- FDA should establish clear definitions to distinguish accessories and components consistent with congressional intent and FDA's broader public health objectives.
- FDA should use a reasonable risk-based approach when establishing which FSPTCA provisions should apply to components and parts.
- FDA should exempt tobacco product accessories from regulation.

A. FDA should establish clear definitions to distinguish between accessories and components consistent with congressional intent and FDA's broader public health objectives

1. The definitions should reflect the statutory framework

To effectively administer the deeming regulation in a way that can be understood by stakeholders, we request that FDA define the following terms in the Final Rule: (1) Finished Tobacco Product; (2) Consumption; (3) Components and Parts; and (4) Accessory or Accessories. The need for regulatory definitions in the context of deemed products, such as e-vapor products, is particularly relevant because the terms component, part, and accessory are used interchangeably in the current marketplace and may have a different meaning in commercial contexts.

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[93] 79 Fed. Reg. at 23179.

[94] *Id.* at 23144 and 23152.

[95] *Id.* at 23153.

As a threshold matter, the definitions must be consistent with the FSPTCA's statutory and regulatory framework. The definition of "tobacco product" in Section 201(rr) of the FDCA, as amended by the FSPTCA[96] provides an appropriate starting point:

> "any product made or derived from tobacco that is *intended for human consumption*, including any *component, part, or accessory* of a tobacco product (*except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product*)" [emphases added].

The tobacco product definition provides insight regarding certain elements that Congress deemed relevant. The phrase "intended for human consumption" suggests that Congress intended FDA to regulate tobacco items that can be consumed or items that directly facilitate consumption of tobacco or tobacco derivatives, such as tobacco-derived nicotine. These items most closely fit the definition of tobacco product and likely have the most direct impact on public health beyond the tobacco or tobacco derivatives themselves. Moreover, the exclusion of non-tobacco raw materials from the tobacco product definition demonstrates Congress' intent that certain materials, including certain components, parts or accessories, are exempt from the statute.

FDA should ensure that the definitions reflect a risk-based approach that considers the foreseeable effect of the definitions on the public health. The regulatory definitions must also be 1) flexible enough to encompass each category of deemed tobacco product, as well as different regulatory requirements that may apply to components and parts within a particular product category; and 2) specific enough to allow both industry and FDA staff, including product application reviewers and field and factory investigators, to readily distinguish regulated items from unregulated items.

2. The definitions of "accessory" and "component or part" distinguish each type of item based on its relationship to the "consumption" of tobacco or tobacco derivatives in a "finished tobacco product"

a. FDA should define the term "finished tobacco product" to differentiate other tobacco products (such as components, parts or raw materials) from tobacco products that are capable of being consumed or are intended for consumption

The term "finished tobacco product" appears in multiple provisions of the FSPTCA and tobacco regulation, 21 CFR Part 1140. The FSPTCA, for example, defines "Tobacco product manufacturer" as "any person . . . . who— (B) imports a *finished tobacco product* for sale or distribution in the U.S."[97] Congress could have used the word "tobacco product" in that definition, but instead chose to use "finished tobacco product." In this context, the word "finished" suggests that the product is complete and ready to be consumed by a human as sold or distributed. In other contexts, FDA has stated that a device that has been manufactured or assembled, and need only to be inspected and tested, or packaged or labeled would be considered a finished device rather than a component, because it is in a form or condition where it could be

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[96] *See* FSPTCA § 101(a) (amending FDCA § 201 to include the term "tobacco product").

[97] FSPTCA § 900(20) (emphasis added).

used for its intended purpose.[98] We believe that this construct is relevant and useful for tobacco products.

We propose that FDA include in the Final Rule the following definition of "finished tobacco product":

> A "*finished tobacco product*" means a tobacco product that is intended[99] for human consumption and is suitable and ready for this intended purpose, regardless of whether it is packaged or labeled.

b. *In defining "consumption" FDA should be guided by the fact that "human consumption" is an essential characteristic of tobacco products*

In the Proposed Rule, for example, FDA stated that an item's role in "consumption" may be relevant to whether it is an accessory or a component.[100] We believe that an item's role in consumption is not only "relevant" but determinative of its regulatory status and the extent to which it should be regulated. At the same time, FDA should define "consumption" flexibly enough to encompass current and possible future routes of consumption for tobacco products. We propose that FDA include in the Final Rule the following definition of "consumption":

> "*Consumption*" means (i) ingestion, (ii) inhalation, (iii) absorption through the skin or mucosa, or (iv) otherwise entering the human body.

c. *FDA should combine "components" and "parts" in a single definition and that definition should not include labeling and packaging*

With respect to "components" and "parts," we believe FDA can interpret the statute to combine both terms into a single definition, provided that its interpretation is reasonable.[101] FDA appears to have combined these concepts in the Proposed Rule[102] but provides no meaningful distinction between the two terms, even though it is soliciting comments on whether it should define them.[103]

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[98] *See, e.g.*, 42 Fed. Reg. 11,988, 12,000 (Mar. 1, 1977) (proposing to define "finished device" to "distinguish between a device and a component"); *see also* 21 CFR § 820.3(l) (defining finished device as any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized.").

[99] In other contexts, FDA has stated that a product's "intended use" determines its regulatory status. "Intended use" is the manufacturer or marketer's "objective intent," which is demonstrated by labeling, claims, marketing materials, or other written or oral statements about the product. *See, e.g.*, 21 CFR § 201.128.

[100] 79 Fed. Reg. at 23153.

[101] In other regulatory contexts, FDA has defined component to include "part." For example, in the medical device context, FDA defined "component" as "any raw material, substance, piece, part, …." 21 CFR § 820.3(c). It appears that FDA has not separately defined the term "part" in the medical device context, but has rather incorporated the term into the Agency's definition of component. (emphasis added).

[102] FDA refers to these terms collectively, explaining that "components and parts covered under this proposal include those items sold separately or as part of kits sold or distributed for consumer use or further manufacturing or included as part of a finished tobacco product," and that "such examples would include … ." 79 Fed. Reg. at 23143.

[103] *Id.* at 23153.

We believe it is unnecessary to distinguish a "component" from a "part" for tobacco products because the ordinary meaning of "part" is a portion of the whole. "Components and parts" appropriately describes materials incorporated into a tobacco product through activities such as manufacture, production, processing, combination, use or repair. The term "components and parts" also describes materials incorporated into the product that affect the characteristics of the finished product, such as its materials, ingredients, design, composition, heating sources or other features, as well as what it generates for human consumption.

FDA should not define "components and parts" to include packaging or labeling as those items do not have a direct or material effect on the consumption of the tobacco product. Further, the FSPTCA and FDCA define both "package" and "label" as separate and discrete terms, not as parts of the "tobacco product" itself. "Package" is defined as the "pack, box, carton, or container . . . [or] wrapping . . . ***in which*** a tobacco product is offered for sale, sold, or otherwise distributed to consumers."[104] The package is thus external to, not part of, the tobacco product. Similarly, "label" is defined as "a display of written, printed, or graphic matter ***upon*** the immediate container of any article."[105] The label is, therefore, something affixed to the container in which an article is sold, not part of the article itself. Both statutory definitions preclude that the package and label are indistinct parts subsumed within a "tobacco product."

The definition of "tobacco product," too, precludes an interpretation that the package or label can be a component or part of a tobacco product. The Act defines a "tobacco product" as "[1] any product [2] made or derived from tobacco [3] that is intended for human consumption, including any component, part, or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product)."[106] The package and label of a product are not themselves (1) a product, (2) made or derived from tobacco, or (3) intended for human consumption. The package and label thus contain none of the attributes identified in the statutory definition of a tobacco product. Rather, they are external to the tobacco product. The definition of "tobacco product" also does not use or otherwise cross-reference the separately defined terms "package" and "label." The definition of component and part should explicitly state that they do not include the already defined, separate "package" and "label."

FDA's definitions in other regulatory contexts also support the view that labels and packaging should be excluded from the definition of component or part. As noted above, FDA's device regulations define "finished devices" to distinguish them from components or parts. A finished device is "any device or accessory to any device that is suitable for use or capable of functioning, *whether or not it is packaged, labeled,* or sterilized."[107] The definition clearly makes a distinction between a device and its label or packaging. It also clarifies that a device is considered "finished" when it is operational. It becomes operational through the integration of components or parts that provide its defining characteristics and are necessary for it to function as intended. FDA's drug regulations contain similar concepts with respect to the "finished

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[104] FSPTCA § 900(13) (emphasis added).

[105] FDCA § 201(k) (emphasis added).

[106] FDCA § 201(rr)(1).

[107] 21 CFR 820.3(l) (emphasis added).

dosage form" of a drug product.[108] In both contexts the label or packaging of the products, while important and separately regulated, are not considered "part" of the product.

Finally, at numerous other places in the statute, Congress indicated that a tobacco product's label and packaging are different from, rather than a "part" of, the product. For example, Section 902 of the FSPTCA contains separate provisions deeming a tobacco product adulterated based on the presence of any "poisonous or deleterious substance" in the product itself or in its packaging; and Section 301(qq) of the FDCA prohibits the creation of counterfeit tobacco products by placing an identification device such as a "label ... upon any tobacco product or container or labeling thereof."

For these reasons, we propose that FDA include in the Final Rule the following definition of "component and part":

> "*Component and part*" means any raw material, additive, substance, piece, item, unit, section, assembly, or sub-assembly that is
>
> (i) intended for incorporation into a finished tobacco product; *and*
>
> (ii) intended to affect or alter the composition or characteristics of tobacco or a tobacco derivative including in smoke, vapor, liquid, or other form; *and*
>
> (iii) (1) not otherwise an accessory; and (2) not labeling or packaging.

Examples of components[109] include, but are not limited to: filters, tubes, flavorings, nicotine solutions, cartridges or cartomizers for e-vapor products, heating coils, silica wick assemblies, "tank systems," drip tips, and atomizers.

d. An "accessory" should be defined as a tobacco product only if it is directly involved in or essential to facilitating the consumption of tobacco or tobacco derivatives and should not include labeling or packaging

An item should be a tobacco product only if it is directly involved in or essential to facilitating the consumption of tobacco or tobacco derivatives, such as tobacco-derived nicotine. To differentiate accessories from components and parts, the definition of accessory should exclude tobacco and tobacco derivatives to address the potential tension between the tobacco product definition, which defines accessories as tobacco products,[110] and the Proposed Rule, which would exclude them from regulation under the FSPTCA for deemed tobacco products. The definition of accessory should also exclude labeling or packaging. Tobacco product labeling and packaging are separately defined and regulated under the FSPTCA.[111] Because FDA does not intend to regulate accessories under the FSPTCA, the Agency should clarify that the labeling or packaging of tobacco products are not included in the definition of accessory. In addition, the

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[108] *See* 21 CFR § 210.3(b)(4) (defining drug product as "Drug product" as "a finished dosage form, for example, tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients. The term also includes a finished dosage form that does not contain an active ingredient but is intended to be used as a placebo."). The definition does not include label or package.

[109] 79 Fed. Reg. at 23143.

[110] FDCA § 201(rr).

[111] *See* FSPTCA § 903(a) (specifying contents for tobacco product packaging).

definition of accessory should also ensure that currently regulated consumer products that are not primarily intended for use with tobacco products are not affected by the Proposed Rule, the FSPTCA or the tobacco regulation's sales and marketing restrictions. For example, FDA should not classify as tobacco product accessories items such as lighters, alkaline batteries, dripper tip bottles, cotton swabs and cleaning solutions, and display cases.

> An "*accessory*" means an article that is solely designed and intended for use with a finished tobacco product but is
>
> (i) not made or derived from tobacco; *and*
>
> (ii) not intended to affect or alter the composition or characteristics of what is consumed from use of the finished tobacco product; *and*
>
> (iii) not labeling or packaging.

An electrically powered charger, for example, that is deliberately designed and produced so that it can only be used to charge an electronic component of a tobacco product, such as the rechargeable battery in an e-vapor product, would be an accessory under this definition. Examples of accessories from the Proposed Rule[112] that would be not be accessories under this definition include, but are not limited to, hookah tongs, charcoal burners and holders, cigar foil cutters, humidors, and carriers, as well as items used in the storage or personal transportation of a proposed deemed product such as cases, containers, bags, or other accessory holders (*e.g.*, display or rack). These items are not solely designed and intended for use with a finished tobacco product and, therefore, do not meet the above definition for "accessories."

B. FDA should use a reasonable risk-based approach when establishing which FSPTCA provisions should apply to components and parts

FDA's approach to regulating components and parts should be transparent and grounded in sound scientific and legal principles. The Agency should consider the relative risks posed by various types of components and parts under specific conditions of use or through specific distribution channels and impose the least burdensome requirements necessary to effectively manage or mitigate those risks. In determining the appropriate regulatory approach for components and parts, FDA should consider: (1) whether the item could affect or alter the tobacco product; (2) whether it is directly involved in consumption; (3) whether it is immediately necessary for the intended use of the product; (4) whether it is intended for further manufacture or distribution or sale to consumers; and (5) the foreseeable potential effect of the item on public health.

This regulatory approach is consistent with sound risk-based principles for the regulation of other products distributed or sold to consumers. It is also consistent with the statutory framework for tobacco products, which excludes from the definition of tobacco product certain non-tobacco raw materials used to manufacture tobacco components.[113]

Such a regulatory approach also aligns with FDA's current strategy for reviewing component information in premarket authorization applications. For example, FDA's Draft and Final

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[112] 79 Fed. Reg. at 23143. FDA included some of these examples in the Proposed Rule.

[113] *See* FDCA § 201(rr).

Guidance documents on PMTAs and SE notices explain that FDA does *not* intend to enforce the requirements of either Section 910 or 905(j) of the FSPTCA for components of regulated tobacco products that are sold or distributed solely for further manufacturing into finished tobacco products because the Agency anticipates "receiving relevant information regarding such new tobacco products in the PMTA submission for the finished regulated tobacco products."[114] Further, in its SE Guidance, FDA recommends that tobacco manufacturers include in their submission a listing of (1) design features; (2) ingredients; and (3) materials, components and subcomponents (if applicable), as well as a description of the heating source used in the consumption of the finished tobacco product. We believe that allowing finished product manufacturers to provide information regarding components and parts in SE or PMTA submissions gives FDA relevant information regarding the components and parts used to make "new tobacco products."

1. FDA should apply all applicable FSPTCA requirements to tobacco components and parts intended to be sold directly to consumers

FDA should subject manufacturers of components and parts that are made of, derived from, or contain tobacco or tobacco derivatives, such as tobacco-derived nicotine ("tobacco components and parts") and are intended to be sold directly to consumers to all applicable FSPTCA requirements. This approach is reasonable and consistent with the intent of the FSPTCA because components and parts that contain tobacco or tobacco derivatives arguably also meet the statutory definition of tobacco product, subjecting them to all provisions of the statute.

For example, it is reasonable for FDA to require pre-filled e-vapor cartridges and "tanks", "tank systems", bottles of nicotine or e-cigarette cartomizers (that have tobacco or tobacco-derived nicotine) sold directly to consumers to have tobacco product labeling and warnings. In addition to tobacco warnings, FDA should also consider whether "tanks" or "tank systems" should include (1) information about the heating mechanism (coil) and energy source (battery); (2) information about overheating or overuse, including risk of fire (if applicable); (3) warnings or precautions about use in or near water as well as any electrical shocks; and (4) warnings and instructions about replacing components and parts. Filled "tanks" or "tank systems" should also be subject to age and identification restrictions in the absence of evidence of a non-tobacco intended use.

Moreover, the premarket authorization requirements should also apply to such products taking into account the aerosols or vapors generated when consumers use such tobacco components and parts. Further, FDA should adopt, for example, similar standards for leachable and extractable analysis requirements as those currently used for medical devices (*e.g.*, International Conference on Harmonization ("ICH") Q3B and Q6A). For products that have electrical components, FDA should consider recognizing applicable consumer electrical safety and performance standards or those applied to similar electronic products of similar power ratings. Such standards include requirements for systematic evaluation of electrical product hazards, electromagnetic compatibility and interference, battery safety and good electronic design practices.

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[114] Draft Guidance for Industry Applications for Premarket Review of New Tobacco Products (Sept. 2011) at 4; Draft Guidance for Industry and FDA Staff Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions (Sept. 2011) at 5.

2. FDA should apply certain FSPTCA requirements to tobacco components and parts intended solely for further manufacture of other tobacco products

FDA should require manufacturers of tobacco components and parts that are intended for further manufacture (*e.g.*, incorporated into a finished tobacco product) to comply with the (i) FSPTCA registration and listing requirements and (ii) existing product performance or quality standards, such as international or national consensus standards recognized by FDA or other regulatory authorities.

FDA should not require manufacturers of tobacco components and parts that are intended for further manufacture to comply with the tobacco regulation's labeling, warnings and marketing and sales restrictions because, although such items would contain tobacco or tobacco derivatives, they would be intended for further manufacture and ultimately be incorporated into a tobacco product intended for distribution or sale to consumers. The tobacco product itself would contain the required labeling and warnings as well as be subject to the applicable tobacco regulation's marketing and sales restrictions. Instead, FDA could require such manufacturers to ensure that all components and parts that contain tobacco or tobacco derivatives are shipped and packaged with labeling that indicates that they are intended for further manufacture. FDA could then enforce these requirements through audit or inspection.

Tobacco components and parts that are intended for further manufacture also should not be subject to any new or additional product or safety or performance standards because the manufacturer of the final tobacco product distributed or sold to consumers will incorporate and certify to such safety and quality measures in their premarket authorization applications. Finally, tobacco components and parts that are intended for further manufacture should not be subject to premarket authorization requirements because FDA will review them as part of the SE reports or PMTAs for the final tobacco product distributed or sold to consumers.

3. FDA should apply certain FSPTCA requirements to non-tobacco components and parts intended to be sold directly to consumers

FDA should require manufacturers of non-tobacco components and parts that are sold directly to consumers to be subject to the following FSTPCA requirements: (i) registration and listing requirements; (ii) ingredients and constituents submissions; (iii) packaging labeling and tobacco product warnings; (iv) premarket authorization requirements; (v) existing product performance or quality standards, such as international or national consensus standards recognized by FDA; and (vi) sales and marketing restrictions.

For example, it is reasonable to apply the premarket authorization and constituent reporting requirements to manufacturers of empty "tanks", "tank systems", and other e-vapor components intended for distribution or sale directly to consumers. Such requirements should be applied in a way that accounts for each probable combination of tobacco-derived nicotine-containing liquid and each such empty "tank" or "tank system" and the aerosols produced by such combinations. The properties of the aerosol (*i.e.*, e-vapor) are a function of the e-vapor liquid, the materials that contact both the aerosol and the e-vapor liquid and the energy management of the device (*e.g.*, battery voltage, temperature of the heating coil). For example, increased temperature of the heater coil could result in increased levels of certain chemicals transferring to the aerosol. Consumers are exposed to this aerosol when they use a "tank" or "tank system." The key is analyzing the interaction between a particular liquid and any empty "tank" or "tank system" in

which that liquid could be used and the interaction between a particular "tank" or "tank system" and any liquid which could be used therein.

FDA should also apply to empty "tanks" and "tank systems" the same leachable and extractable analyses requirements, the adoption of electronic safety standards, and the requirement that manufacturers provide certain information to consumers as suggested above for filled "tanks," "tank systems" and cartomizers.

4. FDA should apply certain FSPTCA requirements to non-tobacco components and parts intended solely to be distributed for further manufacture

Manufacturers of non-tobacco components and parts intended solely for distribution for further manufacture of other tobacco products should be subject to only the registration and listing requirements of the FSPTCA because all other requirements or obligations will be met by the manufacturer of the final tobacco product distributed or sold to consumers.

C. FDA should exempt tobacco product accessories from regulation

We agree with FDA's proposal to exempt accessories of deemed tobacco products from the requirements of the FSPTCA and the sales and marketing restrictions.[115] The FSPTCA was enacted to give FDA authority to regulate the manufacturing, marketing, advertising, and distributing of tobacco products based, in part, on Congressional findings regarding the health risks of these products.[116] However, Congress recognized that effective tobacco regulation requires a balanced, objective and scientifically sound approach in which the type and scope of regulation is determined based on the relative risks of the particular product. Accessories, as defined in this comment, do not have the same attributes, and therefore, do not present the same risks as currently regulated tobacco products or those addressed in the Proposed Rule.

Accessories include a variety of non-tobacco items and consumer goods that are used primarily for convenience, efficiency, or personalization. Items such as bags, cases and humidors provide a convenient way for ATCs to store and transport tobacco products when they are not in use. USB chargers and wall adapters allow for efficient use of e-cigarettes and other e-vapor devices. Digital or electronic trackers that allow consumers, for example, to monitor their battery life or e-vapor liquid levels provide convenience to consumers. Accessories may include carrying cases or storage boxes that contain safety enhancements such as locking mechanisms or digital codes designed to prevent youth access.

Unlike currently regulated tobacco products, accessory items do not contain tobacco or tobacco-derived nicotine and are not intended to affect or alter the composition or characteristics of what is consumed from use of the finished tobacco product. The labeling and warning, premarket authorization, ingredients submission, other requirements of the FSPTCA, and the sales, advertising and marketing restrictions in 21 CFR Part 1140 are designed to address the health risks and potential population harms associated with human consumption of tobacco products. These requirements are not effective or appropriate for accessories. Indeed, the absence of tobacco and the possibility of human consumption appear to have weighed heavily in FDA's

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[115] 79 Fed. Reg. at 23178.

[116] *See* FSPTCA § 4.

decision to exclude accessories from FSPTCA and tobacco regulation requirements. In the Proposed Rule, the Agency states that accessories will "have little impact on the public health" since accessories are "not included as part of a finished tobacco product" and "are not expected to be used in the consumption of a tobacco product."[117] Therefore, FDA should not restrict the extent to which tobacco accessories can bear or contain brand names or trade names for tobacco products. The use of tobacco product brand and trade names is appropriate and necessary to identify accessories that are designed for use with certain brands of tobacco products.

Many accessories, moreover, are consumer products and are already regulated by agencies such as the Consumer Product Safety Commission ("CPSC") or subject to national and/or international consensus standards that establish standards for the manufacture, labeling, distribution and disclosure of safety risks, warnings, and other information relevant to the consumer. FDA should not impose new burdens, performance standards or novel requirements on accessories such as chargers or cases simply because they are intended for use in connection with tobacco products.

Finally, as previously noted, FDA should not define accessories so broadly that it inadvertently affects or alters the regulatory status of ordinary consumer products which are primarily designed or intended for use with nontobacco products. For example, FDA should not classify all lighters as tobacco accessories because not all lighters are designed or intended solely for use with combustible tobacco products. Some lighters, for example, are specifically designed to light candles, barbeque grills, and campfires while other general purpose lighters can be used for these purposes as well as lighting cigarettes, cigars and/or pipe tobacco.

Moreover, certain products that are designed for use with a tobacco product are already regulated as consumer products under the Consumer Product Safety Act ("CPSA").[118] CPSC, for example, regulates child resistant cigarette lighters.[119] Our proposed definition of "accessory" is also consistent with the regulation of cigarette lighters by the CPSC, in light of the CPSA's exclusion of "tobacco products" from the jurisdictional scope of the CPSC.[120]

Therefore, it is important for FDA to not inadvertently pull such items into the definition of accessories.

FDA has discretion to adopt the definitions and implement the regulatory framework we propose. By defining and distinguishing accessory, components and parts and related terms,

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[117] 79 Fed. Reg. at 23143 and 23153.

[118] 15 U.S.C. § 2051(b).

[119] 16 CFR Part 1210 (safety standard for cigarette lighters).

[120] CPSC regulations define "lighter" as follows: "Lighter, also referred also referred to as *cigarette lighter*, means a flame-producing product commonly used by consumers to ignite cigarettes, cigars, and pipes, although they may be used to ignite other materials."[120] Under the definition of "accessory" proposed above, such a lighter would not be an accessory because it is not designed or intended "solely" for lighting a tobacco product. Since such a lighter is not an accessory, it would not be a tobacco product. The CPSC determined that it has jurisdiction to issue these regulations, despite the fact that the CPSA excludes tobacco products from CPSC's jurisdiction, because such lighters are not tobacco products. Our definition would comport with CPSC's determination and Congressional intent by continuing to exclude such lighters from the definition of tobacco product as used in both the CPSA and the FSPTCA.

FDA would effectively address the relative risks of various products and avoid inappropriate, burdensome regulation. The adoption of clear and flexible definitions and the regulatory approach we propose appropriately focuses and applies FDA regulatory oversight on items that could impact public health. These definitions would also promote the FSPTCA's objectives, avoid impractical outcomes, and promote certainty and efficiency.

Section VI. FDA Should Establish Product Pathways that Encourage Innovation of Potentially Reduced Harm Products and Provide a Feasible Process to Market Such Products

We support FDA's effort to regulate deemed tobacco products and encourage FDA to create an appropriate regulatory framework, consistent with sound scientific principles and legal requirements. We believe that FDA should exercise its statutory authority and discretion to develop tailored regulatory approaches for deemed tobacco products that will comply with the FSPTCA's requirements and reduce the harm caused by tobacco use.

As proposed, the rule provides two product pathways by which a manufacturer can obtain market authorization: SE or PMTA. The proposed rule, however, also maintains the February 15, 2007 "grandfather date" for establishing predicate products that apply to the SE pathway. FDA correctly recognizes that "for some products, there may not be predicate products that were on the market as of February 15, 2007, to which to claim substantial equivalence" particularly for "e-cigarettes and similar novel products."[121] FDA specifically requested comments on "whether and, if so, how [it] should consider a different regulatory mechanism for newer proposed deemed tobacco products that cannot, as a practical matter, use the [SE] pathway."[122] FDA also asked if there "are other legal interpretations of the substantial equivalence grandfather provision that FDA should consider."[123] FDA has also acknowledged "the existence of a continuum of nicotine-delivering products that pose differing levels of risk to the individual"[124] and asked for comments about how e-vapor products should be regulated based on this continuum.[125]

We urge FDA to implement product pathways that are the least burdensome approach[126] to regulation, comply with the requirements of the FSPTCA and support manufacturers' efforts to develop and bring to market innovative potentially reduced risk products.

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[121] 79 Fed Reg. at 23145; *see also id.* at 23176 ("FDA is not certain that manufacturers would in fact be able to use the SE pathway for many proposed deemed tobacco products because they may not be able to identify a viable predicate.").

[122] *Id.* at 23144.

[123] Id. at 23176.

[124] *Id.* at 23147.

[125] *See id.* at 23152.

[126] For example, FDA applies the "least burdensome" approach concept in the medical device context as "a successful means of addressing a premarket issue that involves the most appropriate investment of time, effort, and resources on the part of industry and FDA." FDA, "Final Guidance For FDA and Industry: The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles" (Oct. 2002).

Accordingly, our comments in this section address the following points:

- Application of the SE and PMTA requirements, as proposed, to deemed tobacco products would be inconsistent with Congressional intent and could limit the availability of potentially reduced risk products.
- FDA should exercise its statutory authority and discretion to preserve Congress' intent regarding the SE pathway for deemed tobacco products.
- FDA should use its statutory authority to implement accelerated or modified PMTA pathways for deemed tobacco products.
- FDA must consider and, when appropriate, adopt alternatives to the Proposed Rule in order to avoid infirmities under the Administrative Procedure Act ("APA") and the U.S. Constitution.

A. Application of the SE and PMTA requirements, as proposed, to deemed tobacco products would be inconsistent with Congressional intent and could limit the availability of potentially reduced risk products

The FSPTCA reflects Congress' desire to "continue to permit the sale of tobacco products,"[127] subject to reasonable controls and appropriate regulatory oversight. Accordingly, Congress created two distinct pathways for bringing to market "new tobacco products": the SE pathway and the PMTA pathway.[128]

In creating the SE pathway, Congress clearly intended that manufacturers should have a meaningful pathway to market, other than the PMTA process, for certain new products that do not raise different questions of public health. Congress also created the SE pathway as *the* mechanism for clearing products already in the market when such products become subject to FDA regulation.[129] By contrast, Congress intended a separate pathway for initial entrants into the market post regulation. This separate pathway, the PMTA pathway, contemplates additional evidentiary requirements for applicants. Because Congress intended PMTAs for truly new, not previously marketed products, manufacturers will not—by definition—have market-use data to satisfy pre-market requirements. The Proposed Rule, however, undermines this statutory framework and disregards Congressional intent by effectively foreclosing e-vapor products from using the SE pathway because they were not widely commercially marketed as tobacco products in the United States as of February 15, 2007. In fact, FDA did not even recognize e-cigarettes as "tobacco products" until 2011, when it did so at the direction of the D.C. Circuit.[130] FDA should

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[127] FSPTCA§ 3(7). FDA is expressly prohibited from banning the sale of certain products. FSPTCA § 907(d)(3) (expressly prohibiting FDA from banning "all cigarettes, all smokeless tobacco products, all little cigars, all cigars other than little cigars, all pipe tobacco, or all roll-your-own tobacco products").

[128] *Id.* § 910(a)(3); *see also id.* § 905(j). The FSPTCA also permits FDA to exempt manufacturers from a premarket demonstration of substantial equivalence for products that are minor modifications (*i.e.*, adding, deleting, or modifying the quantity of an existing tobacco additive) of other products, for which an SE report is unnecessary to ensure that permitting the marketing of the product "would be appropriate for the public health." FSPTCA § 905(j)(3); 21 CFR § 1107.1.

[129] *See* FSPTCA § 905(j)(2).

[130] *See Sottera*, 627 F.3d at 897.

use its regulatory authority and enforcement discretion to satisfy Congressional intent and the statute.

FDA should ensure the availability of the SE pathway as a matter of policy because doing so increases the likelihood that potentially reduced risk tobacco products are made available to ATCs.

B. FDA should exercise its statutory authority and discretion to preserve Congress' intent regarding the SE pathway for deemed tobacco products

1. The "grandfather date" for deemed tobacco products should be the date of the Final Rule

Congress clearly intended SE to serve as a valid premarket pathway and *the* pathway for premarket clearance of products in the market at the time they become subject to FDA regulation. The most effective and efficient means for FDA to achieve Congress' intent is to exercise its deeming[131] and regulatory authority[132] and its enforcement discretion[133] by establishing an alternative grandfather date for deemed tobacco products. A logical date would be the effective date of the Final Rule. This would make the SE pathway a viable option for potentially reduced risk products that are already on the market and for which the SE pathway was specifically designed.

Initially, Congress only subjected certain products to the FSPTCA and granted FDA deeming authority to subject additional products to Agency regulation. If Congress intended all tobacco products to be subject to the FSPTCA in the same ways, it would have done so explicitly. Instead, Congress intended that FDA create regulatory frameworks appropriate for each category of deemed products and consistent with the Agency's overall statutory and public health mandates. Further, Congress granted FDA "[t]he authority to promulgate regulations for the efficient enforcement" of the FSPTCA.[134] By granting FDA this authority, Congress intended that the Agency, when promulgating regulations, consider "the statutory scheme as a whole" and "practicalities, such as 'an understanding of what types of enforcement problems are encountered by FDA (and) the need for various sorts of supervision in order to effectuate the goals of the Act.'"[135] In keeping with that general grant of regulatory authority, the FSPTCA is specifically designed to provide FDA with "flexible enforcement authority" to regulate tobacco products

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[131] FSPTCA § 901(b). The FSPTCA provides that the deeming authority delegated to FDA must be exercised "by regulation." *Id.* The statute also requires that each rulemaking "be in accordance with chapter 5 of title 5, United States Code"—*i.e.*, the APA. *Id.* § 901(d).

[132] FDCA § 701(a).

[133] The Supreme Court "has recognized on several occasions over many years that an agency's decision not to prosecute or enforce, whether through civil or criminal process, is a decision generally committed to an agency's absolute discretion." *Heckler v. Chaney*, 470 U.S. 821, 831 (1985). Applying this principle in *Heckler*, the Court held that the FDCA's "enforcement provisions thus commit discretion to the Secretary to decide how and when they should be exercised." *Id.* at 835.

[134] FDCA § 701(a).

[135] *Nat'l Confectioners Ass'n v. Califano*, 569 F.2d 690, 693 (D.C. Cir. 1978) (quoting *Toilet Goods Ass'n v. Gardner*, 387 U.S. 158, 163-64 (1967)).

while "continu[ing] to permit the sale of tobacco products to adults."[136] These provisions show that Congress intended a process in which FDA informs itself, through notice and comment, about regulating particular tobacco product categories and devises a regulatory framework suitable for each category after comprehensively considering alternatives.

FDA's exercise of its regulatory authority and enforcement discretion to change the "grandfather date" to the date of the Final Rule would also be consistent with similar actions that FDA has already taken with respect to other tobacco products.[137] Such a straightforward approach would be the most effective way for FDA to make available all of the premarket pathways Congress intended to apply to tobacco products once deemed.

2. FDA has the statutory authority to selectively deem certain tobacco products or deem products for selective purposes

Nothing in the statute requires FDA to engage in all-or-nothing deeming for all purposes. In fact, doing so may not be in the best interests of public health. Rather than deem an entire class of tobacco products categorically subject to the FSPTCA for all purposes, FDA has multiple options for proceeding in a reasoned, scientifically sound, and incremental manner. An incremental approach to deeming—*i.e.*, deeming only certain subclasses of a particular tobacco product subject to the FSPTCA, or deeming only for certain purposes—is consistent with the overall regulatory framework established by Congress, FDA's flexible enforcement authority, and the public health objectives underpinning the FSPTCA.

For e-vapor products and other TDNPs commercially marketed in the United States before the Final Rule, FDA should deem them for the designated purposes under the FSPTCA of age-restrictions, warning labels, and disclosure requirements, without subjecting them to premarket authorization requirements. Such an action would deem only those e-vapor products commercially marketed in the United States after the issuance of the Final Rule to be subject to all aspects of the FSPTCA.

Alternatively, FDA should deem all e-vapor products and other TDNPs, regardless of when they enter the U.S. market, subject to certain sections of the FSPTCA but not the premarket authorization requirements. FDA could achieve its public health objectives by subjecting these products to FSPTCA provisions governing the manufacture, labeling, and sale of the products. This would avoid the difficulties of the premarket review process created by the Proposed Rule, but still allow FDA to monitor products and address compliance issues through post-market enforcement. FDA has adopted a similar approach for products such as dietary supplements and certain over-the-counter drugs that are not subject to pre-market review requirements, but must

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[136] FSPTCA § 900 (note).

[137] *See, e.g.*, 79 Fed. Reg. at 23145 ("FDA does not intend to initiate enforcement action against products on the market for failing to have an FDA marketing authorization until 24 months following the effective date of the final rule."); FDA, "Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act" (Mar. 2012), http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm297752.htm ("FDA recognizes that industry may be unable to meet the deadline due to current testing limitations . . . . FDA intends to exercise enforcement discretion to require reporting about only these 20 constituents this year."); *see also* 77 Fed. Reg. 27591 (May 11, 2012) (delaying compliance dates for the final rule regarding labeling of over-the-counter sunscreen products).

comply with other requirements to ensure that consumers and FDA have relevant information. The European Union has also adopted a similar framework for e-vapor products and there is no reason why this regulatory strategy could not work here. For example, under the European Union framework e-vapor products are essentially treated as consumer products that do not require pre-market authorization. A manufacturer is required, however, to provide pre-market notification and submit certain data. The products are also subject to requirements that provide regulators with a reasonable degree of oversight for the products after they enter the marketplace. Specifically, the products are subject to rules governing how they are manufactured, produced, presented, and sold.[138] A similar approach here would be fair, efficient and protective of the public health. If, after additional time and in-market experience, FDA determines that e-vapor products should be subject to premarket authorization pathways, including the SE pathway, FDA could use its rulemaking authority to deem them subject to such requirements.

3. FDA should ensure that the SE pathway remains available by broadly defining the relevant characteristics for predicates

In determining whether a tobacco product is substantially equivalent to predicate products, manufacturers and subsequently FDA compares the products' characteristics.[139] "Substantially equivalent" does not mean identical, but rather affords FDA a measure of judgment to determine the relevant similarities between two products—materials, ingredients, design, composition, heating source, or other features of a tobacco product.[140] FDA should exercise its interpretive authority to define broadly through regulation or guidance when products are sufficiently similar to satisfy the requirements of substantial equivalence. For example, assuming for the sake of argument that there were no valid *predicate e-vapor products* available as of February 15, 2007, there may be other predicate tobacco products sufficiently similar to the e-cigarettes on the market today with respect to characteristics that FDA identifies as relevant for SE comparisons.

Additionally, the SE pathway is available for tobacco products that, although not sharing the same characteristics of a predicate product, "do[] not raise different questions of public health."[141] The statute does not define what constitutes "different questions of public health" nor has FDA issued regulations defining the phrase. FDA should issue regulations or guidance defining when a new tobacco product does not raise *different questions of public health.* Such regulation should clearly draw comparisons between the public health profiles of products. This regulatory clarity would facilitate the identification of predicates even where there are no *specific* original products on the market from which the new product was directly derived. Thoughtfully executing this approach would provide a practical mechanism to ensure the availability of the SE pathway for e-vapor product manufacturers.

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[138] Tobacco Products Directive (2014/40/EU).

[139] FSPTCA § 905j(a)(3)(A)-(B).

[140] *Id.*

[141] FSPTCA § 905j(a)(3)(A)(ii).

C. FDA should use its statutory authority to implement accelerated or modified PMTA pathways for deemed products

Alternatively, FDA should modify its PMTA pathway for e-vapor products and other TDNPs to avoid foreclosing – as a practical matter – the SE pathway. In the past, FDA has similarly used its statutory authority and discretion to develop flexible approval policies, modified processes, and non-enforcement policies for certain classes of drugs, medical devices, and other products.[142] Consistent with these approaches, FDA should employ such strategies to foster important public health goals, avoid impractical outcomes, encourage innovation of new products, and promote fairness and efficiency in certain deemed tobacco product categories such as those that are non-combustible and potentially less harmful.[143] Specifically, and as detailed below, FDA should consider creating an accelerated review process and/or a product and performance standards process for deemed tobacco products.

1. FDA should implement an accelerated PMTA pathway

Congress recognized that the diversity of new tobacco products may require different approaches to testing and analyzing scientific information in PMTAs. Section 910(c)(5)(B) expressly grants FDA discretion regarding what scientific evidence to accept in evaluating tobacco product applications, and authorizes the Agency to accept evidence other than that derived from well-controlled investigations.[144] Thus, FDA should create an accelerated PMTA process, determining that for products already on the market, certain evidence other than well-controlled clinical investigations is "sufficient to evaluate the product."[145]

To implement an accelerated PMTA pathway, FDA should issue regulations or guidance defining particular evidentiary requirements and criteria. For example, FDA might allow applicants to submit studies using surrogate endpoints, case reports, or retrospective analyses. FDA's guidance or regulation could set specific parameters for these tests and evidence. Such tests and evidence requirements, for e-vapor products and individual components sold to consumers, as an example, could comprise nicotine pharmacokinetics, toxicological assessments (including *e.g.*, data on leachables and extractables), and chemistry/constituent analyses of the e-vapor or aerosol. The abbreviated requirements should reflect FDA's determinations about what

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[142] For example, FDA generally has exercised enforcement discretion in the context of lab-developed tests because they are considered low-risk and serve public health goals. *See* Transcript of FDA Public Meeting on Oversight of Laboratory Developed Tests, Monday, July 19, 2010, *available at* http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM226203.pdf, 8-22[hereafter Transcript]; FDA, "Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays." FDA also has chosen not to regulate certain mobile applications that come within its jurisdiction. *See* FDA, "Guidance: Mobile Medical Applications" (Sept. 25, 2013) at 4, *available at* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf.

[143] *See* FN 126, *supra.* In the device context, FDA seeks to consider the "least burdensome approach" to regulation and compliance with the relevant scientific and legal requirements.

[144] "If the Secretary determines that there exists valid scientific evidence (other than evidence derived from investigations . . . which is sufficient to evaluate the tobacco product, the Secretary may authorize that determination . . . be made on the basis of such evidence."

[145] FSPTCA § 910(c)(5)(B).

evidence is sufficient to demonstrate that marketing a product is "appropriate for the protection of the public health."[146]

FDA uses a similar abbreviated process in other contexts. For example, FDA permits the use of surrogate endpoints and biomarkers under its accelerated approval process for certain drug products.[147] FDA has explained that accelerated drug approval does not reduce the quantum or quality of evidence, but rather that the evidence the Agency accepts satisfies the statutory standard.[148] Similarly, in the context of tobacco products, FDA also should impose post-marketing data requirements on products approved under accelerated PMTAs to confirm its conclusions about individual and population risks and benefits including consumer use patterns.

2. FDA should establish a tobacco product and performance standards system as an alternative, or in addition to, an accelerated PMTA pathway

FDA should simplify the PMTA process by establishing clear, meaningful and achievable performance standards that would ensure market authorization of qualified tobacco products.

Sections 910 and 907 give FDA the authority to establish a framework of product or class-specific performance standards (hereinafter "Standards"). FDA should exercise its authority under Section 907(a)(3) to create specific baseline Standards for each category of deemed tobacco products or for certain categories, such as e-vapor products. The Standards would then serve as the bases for an abbreviated or alternative marketing authorization pathway by which deemed products could satisfy the statutory PMTA requirements. Such a result is supported by the FSPTCA, which clearly reflects Congress' intent that different levels of regulation would be appropriate for different categories of products.[149] This regulatory pathway also is scientifically sound, and consistent with FDA precedent for non-tobacco products.[150]

FDA should issue an Advance Notice of Proposed Rulemaking to collect data for creating Standards for deemed tobacco product categories. For example, FDA could request data from manufacturers, including importers, related to factors such as the ingredients, chemical or

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[146] FSPTCA § 910(c)(5)(A).

[147] *See* 21 CFR Part 314, Subpart H.

[148] The preamble to the Subpart H regulations addressed comments that the rule established "a standard for the evaluation of drug product effectiveness that is inconsistent with the substantial evidence requirement of section 505(d) of [the FDCA]": FDA responded that the "evidence available at the time of approval under this rule will meet the statutory standard, in that there must be evidence from adequate and well-controlled studies showing that the drug will have the effect . . . in its labeling . . . . While the act does not refer to particular endpoints or state a preference for clinical, as opposed to surrogate, endpoints, it is well established that the effect shown in well-controlled studies, must, in the judgment of the agency, be clinically meaningful." 57 Fed. Reg. 58942 (Dec. 11, 1992).

[149] For example, FSPTCA § 907(a)(1)(A), establishes special rules for cigarettes, § 907(e) specifically addresses menthol cigarettes, and § 907(f) specifically addresses dissolvable tobacco products. Additionally, § 911 establishes a separate regime for "modified risk" tobacco products.

[150] For example, FDA has created an alternative approval pathway for medical devices conforming to FDA-recognized technical specifications and performance standards. FDA, "Guidance for the Industry and FDA Staff: Recognition and Use of Consensus Standards," (Sept. 17, 2007), *available at* http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077274.htm (stating "CDRH believes that conformance with recognized consensus standards can support a reasonable assurance of safety and/or effectiveness for many applicable aspects of medical devices").

constituent analyses of the vapor/extract to be consumed, instructions for use, quality, performance, and other characteristics relevant to each category.[151] Standards would delineate the types of evidence or testing criteria required to demonstrate that each product meets the Standards tailored to the specific category (*e.g.*, device components, e-vapor liquid contents, and individually sold e-vapor liquids or devices).

Once FDA has established product or class-specific baselines and Standards, FDA could begin to apply premarket authorization requirements for those deemed tobacco product categories based on the science and evidence. If an individual product complied with the relevant final Standards then it would represent FDA's determination that the product satisfies the PMTA requirements. Each final Standard would be codified in a specific "performance standard" regulation, under a new tobacco subpart of 21 CFR. FDA would update Standards as needed to add, change, or remove criteria. Additionally, interested parties could petition FDA for review and amendment of Standards, for example, through a citizen petition.[152]

Once FDA has established the final Standards regulation for a particular tobacco product category, such as e-vapor products, FDA would start accepting applications for currently marketed or deemed products within 90 days of implementing the Standards regulation(s). A currently marketed product could remain on the market while FDA reviews the application for that product.[153]

Thereafter, manufacturers would submit applications 90 days before they intend to commercially market a product. Specifically, manufacturers would submit reports demonstrating that their products conform to the Standards and FDA would consider whether the submitted documentation is acceptable to demonstrate conformance with the Standards. Products that satisfy the Standards would be *per se* appropriate for the protection of public health and thus receive a marketing order. If FDA determined that a product did not conform to the Standards, it would issue an order to discontinue the sale of that product.

Manufacturers of products that satisfy the Standards, but have certain different or additional attributes not covered by Standards, would submit abbreviated PMTAs, providing the information on the additional attributes.

3. In establishing baseline product and performance standards, FDA should apply a science- and evidence-based approach

In establishing baseline product and performance standards for TDNPs, FDA should apply the same sound scientific approach that it currently uses to regulate foods, medical devices,

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[151] FSPTCA Section 907(6) instructs FDA to "endeavor to . . . invite participation, through joint or other conferences, workshops, or other means, by informed persons representative of scientific, professional, industry, agricultural, or consumer organizations who in the Secretary's judgment can make a significant contribution."

[152] This parallels FDA's process for over-the-counter drug monographs. *See* FDA, "Over-the-Counter (OTC) Drug Monograph Process," *available at* http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm317137.htm.

[153] For example, FDA exercised its discretion to enforce against certain currently marketed products when it required hydrocodone-containing antitussive drug products to obtain new drug approvals. *See* 72 Fed. Reg. 55780 (Oct. 1, 2007).

pharmaceuticals and other consumer packaged goods.[154] While a need for population effects research remains, FDA should consider the currently available science suggesting that the use of TDNPs likely presents significantly lower health risks than does the use of combustible tobacco products, such as cigarettes. FDA should, therefore, establish appropriate baselines for TDNPs that recognize both the absolute and relative risk that using such products may pose to human health in the context of the continuum of risk.

For example, in the e-vapor product category FDA should consider three distinct facets, each of which is critical to establishing baseline product and performance standards: 1) e-vapor liquids; 2) e-vapor devices; and 3) e-vapor products including complete systems with both the liquid and a device in a single unit as well as individually sold e-vapor devices and individually sold e-vapor liquids.

a. E-vapor liquids

FDA should establish product standards that, at minimum require the highest available purity for each ingredient used in an e-vapor liquid formulation (*e.g.*, tobacco-derived nicotine, aerosol formers, flavors). For example, the nicotine and the aerosol formers (*e.g.*, propylene glycol and glycerin) should be U.S. Pharmacopeia ("USP") grade. Additionally, all flavor ingredients should be both generally recognized as safe ("GRAS") for use in food and meet the specifications of the Food Chemicals Codex. As it does with tobacco products already regulated under Section 904, FDA should require each manufacturer to report ingredients used in the production of the e-vapor liquid.

The ingredients used in the e-vapor liquid, particularly nicotine, may degrade over time while the e-vapor product is manufactured, shipped and available at retail. So any product standard established by FDA should require manufacturers to demonstrate the stability of their e-vapor liquid formulation through its projectable commercial life. FDA guidance Q3B(R2)-Impurities in New Drug Products would serve as an appropriate guide for establishing nicotine degradant concentration limits.

The FDA established product standard should also require manufacturers to demonstrate that any flavor ingredient added to an e-vapor liquid does not increase the inherent toxicity of the baseline e-vapor liquid. FDA recognizes that GRAS status and USP grade alone are not necessarily sufficient to assess the potential toxicological impact of e-vapor liquid flavor ingredients on human health. Manufacturers could use a tiered approach, similar to that described in the FDA Redbook for foods,[155] to demonstrate that a flavor ingredient does not increase the inherent toxicity of the baseline e-vapor liquid. Under such an approach, the potential human exposure to a flavor ingredient would suggest the appropriate level of scientific rigor (*i.e.*, Concern Level)

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[154] The principles of the process we propose can provide a sound scientific basis for many decisions that FDA should make as it regulates deemed products. Thus, even if FDA declines to adopt this process as a basis for baseline product and performance standards, it should consider its applicability in other contexts – for example, as a basis for determining whether a tobacco product has been modified, whether the different characteristics of a new tobacco product raise different questions of public health, or whether an exemption from substantial equivalence requirements applies.

[155] U.S. FDA. Office of Food Additive Safety Redbook 2000.

necessary to demonstrate that the intended use of the ingredient is appropriate and meets the standard.

E-vapor generated from the e-vapor liquid is ultimately consumed. As a result, any product standard should require manufacturers to demonstrate that flavor ingredients delivered in the aerosol (*i.e.*, e-vapor) do not cause route-of-exposure-specific effects. For example, e-vapor liquid flavor components should be interrogated by toxicological studies that are not only dependent on the flavor *per se*, but are representative of how humans will be exposed to the flavor through use of an e-vapor product (*e.g.*, aerosol particle size, aerosol particle size distribution, temperature of e-vapor liquid at heating source). *In-vitro* assays using aerosol from the e-vapor product, 90-day rodent inhalation studies, or a combination of assays that may predict toxic effects in the respiratory tract or systemic toxicity as a result of inhalation exposure to the aerosol may prove sufficient. As previously noted, the aerosol is a product of the interaction of a specific e-vapor liquid with a specific device. Each combination of e-vapor liquid and device is not necessarily predicted by the results from the interaction of a single e-vapor liquid and a single device. While FDA should establish product standards requiring manufacturers to demonstrate that e-vapor liquid flavor ingredients are acceptable for their intended use (*i.e.*, that they do not increase the inherent toxicity of the baseline e-vapor product), the standards should not be so prescriptive as to preclude flexibility, such as reliance on in-vitro assays that mitigate the need for in-vivo animal testing.

b. E-vapor devices

E-vapor devices comprise dozens of individual materials and components such as gaskets, wicks, coils, and metal containers. Product standards should require each manufacturer to demonstrate that their device components *per se* do not increase the inherent toxicity of the e-vapor product relative to the baseline. For example, manufacturers should be required to describe the function and composition of each component of their device. In addition, FDA should establish standards for the use of certain device components (*i.e.*, lead solder). Further, as with certain medical devices, there is the potential for e-vapor liquids to extract or leach chemicals from some device components. A product standard should include leachable and extractable analyses requirements similar to those currently used for medical devices (*e.g.*, ICH Q3B and Q6A).

c. E-vapor products (e-vapor liquid + device)

The interaction of the device and the e-vapor liquid is critical to assessing the toxicity of the aerosol from an e-vapor product. FDA should, therefore, establish product performance standards that require a thorough characterization of the aerosol generated from each e-vapor liquid and each device that could be used in combination. This characterization should include product performance characteristics related to an aerosol's potential to directly impact overall human exposure during product use (*e.g.*, the temperature of the liquid at the coil, the particle size distribution of the aerosol, and identification and toxicological characterization of any chemicals formed during the vaping process). For e-vapor liquids and devices sold separately, manufacturers should demonstrate that each possible combination of lawfully marketed e-vapor liquids and device meet the performance standards for the aerosols generated by each such combination.

D. FDA must consider and, when appropriate, adopt alternatives to the Proposed Rule to avoid infirmities under the APA and U.S. Constitution

Under the APA, agency action will be set aside if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law."[156] The APA mandates reasoned regulatory decision-making and requires FDA to gather necessary evidence, consider all aspects of the purported problem, give serious consideration to alternatives, arrive at a reasoned determination, and adequately explain its conclusion.[157] The Proposed Rule fails to take into account the flexibility and regulatory discretion available to the Agency to tailor a regulatory approach that reflects the continuum of risk and the role certain deemed tobacco products, such as e-vapor products, could play in harm reduction. Finalizing the rule as proposed would be an arbitrary and capricious exercise of FDA's authority. It would also raise serious Constitutional questions under the Takings Clause and non-delegation doctrine.

The doctrine of Constitutional avoidance provides an additional reason for the FDA to adopt one or more of the regulatory alternatives we suggest.[158] To the extent there is ambiguity as to the text and structure of the FSPTCA, FDA should strive to "construe [the statute] . . . [to] avoid needless Constitutional confrontations."[159] And to the extent that one or more regulatory alternatives would raise potential Constitutional concerns, the agency should select another option that is unencumbered by similar shortcomings.[160]

FDA's Proposed Rule would pose at least two potential Constitutional difficulties. First, if the SE pathway is foreclosed for e-vapor products, and suitable alternatives are not provided, the regulation could constitute an improper regulatory taking in violation of the Fifth Amendment.[161] Generally, courts apply a three-part balancing test to determine whether a regulatory taking has occurred, asking "(1) what is the economic impact of the regulation; (2) whether the government action interferes with reasonable investment-backed expectations; and (3) what is the character of the government action."[162] Manufacturers of e-vapor products have invested considerable time and resources into developing their products and marketing them in the United States. The e-vapor industry experienced rapid growth prior to FDA's Proposed Rule.[163] The proposed rule has the potential to wipe out significant economic value in derogation of the reasonable expectations of manufacturers of deemed tobacco products. The FDA should avoid such a

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[156] 5 U.S.C. § 706(2)(A).

[157] *See, e.g., Motor Vehicle Mfrs. Ass'n of U.S. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

[158] *See Nat'l Mining Ass'n v. Kempthorne*, 512 F.3d 702, 711 (D.C. Cir. 2008).

[159] *Id.*

[160] *See Hernandez-Carrera v. Carlson*, 547 F.3d 1237, 1250 (10th Cir. 2008) ("[B]oth agencies and courts are obligated to interpret the statute in the one manner that does not raise a serious constitutional question."); *Nat'l Treasury Emps. Union v. Fed. Labor Relations Auth.*, 986 F.2d 537, 540 (D.C. Cir. 1993) ("[The agency] is obliged to consider the possible invalidity of the Statute in selecting between reasonable readings.").

[161] *See, e.g., Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978); *Philip Morris, Inc. v. Reilly*, 312 F.3d 24, 46 (1st Cir. 2002) (en banc) (opinion of Torruella, J.) (holding that a state law that required tobacco companies to disclose their products' ingredient lists effected an unconstitutional taking); *id.* at 48 (Selya, J., concurring in the judgment) (same).

[162] *Id.* at 33 (citing *Penn Cent.*, 438 U.S. at 124).

[163] *See, e.g., Sottera*, 627 F.3d at 892.

Constitutionally problematic outcome by revising the proposed rule to adopt many of the alternative regulatory premarket authorization options described above.

Second, as construed by FDA in the Proposed Rule, the FPSTCA gives the Agency sweeping authority to decide which tobacco products are regulated and which are not without any intelligible principle to guide FDA's deeming. If FDA promulgates a rule that does not apply the reasoned regulatory approach Congress prescribed that takes account of distinctions among tobacco products, it may violate the non-delegation doctrine and contravene principles of separation of powers.

Courts apply the non-delegation doctrine to "giv[e] narrowing constructions to statutory delegations that might otherwise be thought unconstitutional."[164] Applying this principle, the D.C. Circuit has vacated rulemakings that fail to cabin an agency's discretion. In *International Union, United Automobile, Aerospace & Agriculture Implement Workers of America, UAW v. OSHA*,[165] for example, the D.C. Circuit remanded a regulation to the agency for reconsideration because "[t]he claimed power to roam between the rigor of [statutory] standards and the laxity of unidentified alternatives would . . . raise a serious nondelegation issue."[166]

The Proposed Rule's practical effect of denying e-vapor manufacturers a meaningful SE pathway is contrary to the text and the structure of the FSPTCA and arbitrary and capricious. The Proposed Rule also would represent an unreasoned application of FDA's statutory discretion to decide which tobacco products to regulate - a decision that is legislative in nature and that in the normal course, Congress makes after careful and deliberate consideration. To avoid these Constitutional difficulties, FDA should adopt a rule that applies a rational and carefully tailored set of criteria to determine which additional tobacco products should be deemed subject to the Agency's regulatory oversight.

Section VII. Health Warnings Should Be Science- and Evidence-Based, Appropriate to a Product's Risk, and Uniform for all Products in the Same Product Category

A. FDA's proposed warning for e-vapor and other TDNPs is appropriate, but FDA should consider reducing its size

FDA has proposed the following: "WARNING: This product contains nicotine derived from tobacco. Nicotine is an addictive chemical" for all tobacco products that it does not currently regulate, including e-vapor products.

We agree that the content of the proposed addiction warning is appropriate for e-vapor and other TDNPs.[167] To support FDA's commitment to science- and evidence-based decision-making, we

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[164] *Mistretta v. United States*, 488 U.S. 361, 373 n.7 (1989).

[165] 938 F.2d 1310 (D.C. Cir. 1991).

[166] *Id.* at 1318 (observing that the "scope of the regulatory program [was] immense").

[167] The warning would be potentially confusing for tobacco products that contain tobacco leaf. For such products, the nicotine would not be "derived from tobacco" because it naturally occurs and remains in the tobacco leaf used to make them.

attach a bibliography of peer-reviewed published articles that discuss the health risks of nicotine *per se* and such products. (Appendix B).

FDA should, however, reduce the warning size for deemed tobacco products that carry only the addiction warning. For such products, the proposed warning can be clearly and conspicuously communicated to consumers without occupying 30 percent of both principal packaging display panels and 20 percent of advertising space. Requiring warnings larger than necessary to convey the addiction message to consumers would be inconsistent with the First Amendment.[168]

In implementing the proposed warning, FDA should coordinate with other regulatory authorities to harmonize applicable warning requirements and create uniform national warnings for these products.[169] Compliance with FDA's warning requirement should satisfy the requirements of section 903(a)(8) of the FSPTCA.

B. FDA should accept alternative warning sizes, placements, and font sizes for different packaging sizes and configurations so long as the warning is clear and conspicuous

In the Preamble to the Proposed Rule, FDA invited comment on the appropriateness of 30-percent size requirement for product packages.[170] Warnings must be clear and conspicuous, but we urge FDA to be flexible about their size and placement on deemed products, some of which are offered in packaging sizes and configurations very different from cigarette and smokeless tobacco packaging.

Because products like smokeless tobacco have relatively uniform package sizes and configurations, the current CSTHEA warning size requirements work for them. Many of the products that FDA now proposes to deem, however, come in unique shapes and sizes that require diverse –and sometimes very small –packaging. Nu Mark's VERVE® discs, for example, are sold in a small cylindrical package. It is challenging for this type of small packaging to carry brand identification, the required health warning, and other mandated text such as statement of identity, quantity of contents and designated business address. Indeed, for cylindrical packages like those used for VERVE® discs, it is difficult even to identify two "principal" display panels.

Requiring 30% warnings on such packaging would dwarf the branding, potentially violating the First Amendment rule that compelled speech be narrowly tailored to the government interest in

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[168] *See Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980) (for regulation burdening commercial speech to survive, the government must affirmatively prove that (1) its asserted interest is substantial, (2) the restriction directly and materially advances that interest, and (3) the restriction is narrowly tailored).

[169] For example, California's "Safe Drinking Water and Toxic Enforcement Act of 1986," known as Proposition 65 ("Prop 65") "requires businesses to notify Californians about significant amounts of chemicals in the products they purchase, in their homes or workplaces, or that are released into the environment." Cal. Health & Safety Code § 25249.6; *see also* California Office of Environmental Health Hazard Assessment, Proposition 65 in Plain Language, http://oehha.ca.gov/prop65/background/p65plain.html (lasted accessed May 21, 2014). Prop 65 designates nicotine as a developmental toxicant. Manufacturers of e-vapor products that contain tobacco-derived nicotine may therefore be required to communicate a reproductive harm warning to consumers prior to or contemporaneous with their purchase of the product in order to comply with this law. Manufacturers of such products could cause consumer confusion when trying to comply with both FDA's warning requirement and Prop 65 at the same time.

[170] 79 Fed. Reg. at 23164.

disclosing health risks associated with the products.[171] FDA should require no more than the warning be clear and conspicuous in relation to the other communications on the packaging.

FDA has ample authority to recognize differences among products and to adjust the format and type sizes for the label statements accordingly. The FSPTCA authorizes FDA to use rulemaking to modify the "format, type size . . . and text" of package warnings for both cigarettes and smokeless tobacco products.[172] Congress also acknowledged the need to vary warning requirements based on practical constraints. It exempted small point-of-sale cigarette advertisements and cigarette-branded functional promotional items from the Federal Cigarette Labeling and Advertising Act ("FCLAA") warning requirements.[173] At the same time Congress accommodated certain types of newspaper-specific advertising layouts with health warnings of unique dimension.[174] Congress exhibited similar flexibility when it amended FCLAA through the FSPTCA and provided that warning statements required on matchbook advertisements under FCLAA § 4(a) "customarily given away with the purchase of tobacco products" may be printed on the inside cover of the matchbook.[175]

FDA has similarly recognized the need to be flexible. In its Proposed Rule, FDA proposes an exemption from the on-pack warning requirement for cigars sold individually and explained the exemption in the Preamble. "FDA is aware that premium cigars, . . are frequently sold to consumers individually and not in product packaging or an outer covering. Requiring a health warning for cigars that are not sold to consumers in a product packaging, therefore, is impractical."[176] Although we disagree with the proposed exemption and think all tobacco products should be sold with a health warning on the packaging, we agree that FDA should be flexible given packaging constraints.

Finally, FDA should not require manufacturers to use a font size that occupies the greatest possible proportion of the warning area.[177] That proposal is inconsistent with the objective of making the warning clear and conspicuous. A font size that occupies the greatest possible proportion of the warning area will leave limited, if any, white space and may therefore prove to

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[171] *See Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980) (for regulation burdening commercial speech to survive, the government must affirmatively prove that (1) its asserted interest is substantial, (2) the restriction directly and materially advances that interest, and (3) the restriction is narrowly tailored). In addition, the Fifth Amendment prohibits warnings so large that they crowd out trade dress and trademarks, depriving us of their commercial value and resulting in substantial economic loss. The Fifth Amendment Takings Clause prohibits the government from taking private property "for public use, without just compensation." U.S. Const. amend. V, cl. 4. *See also Penn Central Transportation Co. v. City of New York*, 438 U.S. 104, 124 (1978) (When determining whether a regulatory taking has occurred, courts assess (1) the character of the government action; (2) the economic impact of the regulation on the property owner; and (3) the regulation's interference with the property owner's reasonable investment-backed expectations).

[172] *See* 15 U.S.C. § 1333(d), as amended by FSPTCA § 202(b); 15 U.S.C. § 4402(d), as amended by FSPTCA § 205(a).

[173] *See* the 1972 Consent Order entered in the matter of Philip Morris, Inc. before the Federal Trade Commission and the 1980 Consent Judgment in *USA v. Philip Morris, Inc.* Provisions of both were incorporated by reference when Congress amended FCLAA in 1984.

[174] *Id.*

[175] FSPTCA § 201(b)(3).

[176] 79 Fed. Reg. at 23181.

[177] *See* Proposed Rule §§ 1143.3(a)(2)(ii); 1143.5(a)(a)(2)(ii).

be illegible. FDA should thus reduce the warning font requirement to be consistent with smokeless tobacco warnings, which require that the warnings take up 60 to 70 percent of the warning area.[178]

Section VIII. Nu Mark Supports FDA's Proposal to Establish a Federal Minimum Age to Purchase Deemed Tobacco Products

Nu Mark supports FDA's proposal to establish a minimum age of 18 to purchase tobacco products, including e-vapor products. Kids should not smoke or use any other tobacco product. We believe the availability of all tobacco products, including regulated components or parts of e-vapor products sold or distributed to consumers, should be age restricted. FDA's proposal to promulgate a national minimum age for purchase will allow the Agency to apply its resources toward comprehensive enforcement.

Section IX. FDA Should Permit the Distribution of Samples of TDNPs to Age-Verified Adult Tobacco Consumers

FDA should permit sampling of TDNPs to age-verified ATCs, subject to certain restrictions. Sampling could encourage adult smokers to switch to an alternative product within the tobacco category, as well as to switch brands. We encourage FDA to establish a framework that allows for sampling with ATCs, particularly cigarette smokers.

Age-restricted sampling is an important way to educate ATCs about new noncombustible tobacco products. Some ATCs who have tried and rejected e-vapor products in the past and some who have not yet tried e-vapor products say they are unlikely to purchase unless they know more about the product experience, and which types of products best fit with their preferences. Appropriate sampling provides a way for ATCs to learn about and, importantly, try these products. Allowing for appropriate sampling to age-verified ATCs could help accelerate switching smokers to potentially lower risk products and realize potential public health benefits.

For sampling of TDNPs, FDA should require age verification through a face-to-face examination of an ATC's valid government-issued identification.[179] This would be consistent with the approach for smokeless tobacco products. While determining that sampling is inappropriate for cigarettes, Congress allowed smokeless tobacco product sampling in qualified adult-only

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[178] *See* 15 U.S.C. § 4402(a)(2)(B).

[179] FDA has endorsed age verification for tobacco sales by requiring retailers to verify consumers' age through a government-issued identification showing a photograph and at least minimum age. *See* 21 C.F.R. § 1140.14(b). FDA also permits operators of qualified adult-only facilities that offer smokeless tobacco sampling to verify age using government-issued photographic identification cards. *See* 21 C.F.R. § 1140.16(d)(2)(iii)(A) (permitting smokeless tobacco sampling in qualified adult-only facilities that practice age verification based on presentation "to a law enforcement officer (whether on- or off-duty) or to a security guard licensed by a governmental entity of a government issued identification showing a photograph and at least the minimum age established by applicable law for the purchase of smokeless tobacco").

facilities. In addition, Congress empowered FDA to monitor events where sampling occurs and act if FDA finds violations.

Prohibiting samples is "regulation of commercial expression"[180] that the First Amendment permits only if FDA affirmatively proves that (1) its asserted interest is substantial, (2) the restriction directly and materially advances that interest, and (3) the restriction is narrowly tailored."[181] In the past, FDA justified restrictions on cigarette and smokeless tobacco sampling as necessary to prevent youth access.[182] Here, the Agency has offered no government purpose that would be served by preventing manufacturers from providing samples of noncombustible products to ATCs.

FDA must base any sampling ban on science and evidence. At this point, FDA has not shown that sampling is driving youth usage or otherwise undermining public health goals. If sampling TDNPs would help adult smokers to adopt and then switch to potentially lower risk products, then sampling could help achieve public health goals. FDA must present evidence in this rulemaking to justify a total ban on sampling, or its burden will not be met and a separate rulemaking would be required.

Section X. FDA Should Permit the Use of Vending Machines with Electronic Age Verification

FDA's Final Rule should remove the ban on vending machines for deemed tobacco products. Just as the Proposed Rule permits the use of vending machines in facilities that the retailer ensures that no person younger than 18 years of age is present or permitted to enter,[183] FDA should also permit the use of vending machines that utilize effective electronic methods to ensure that only adult consumers can use the machines.

Over recent years, there have been significant technological advancements that allow for accurate non-face-to-face age verification. If vending machines can conduct electronic age and identity verification ("EAIV") by comparing the purchaser's image (captured by the vending machine at the time of sale) with the purchaser's driver's license and perhaps with readily available EAIV data,[184] FDA should permit tobacco product sales through the vending machine.

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[180] *Discount Tobacco City & Lottery, Inc. v. United States*, 574 F.3d 509, 539 (6th Cir. 2012).

[181] *R.J. Reynolds Tobacco Co. v. FDA*, 696 F.3d 1205, 1212 (D.C. Cir. 2012) (citing *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980).

[182] *Id.* 574 F.3d at 539 and 541-42.

[183] *See* Proposed Rule § 1140.41(b)(3).

[184] EAIV compares personal information provided by a consumer against databases that include motor vehicle records, vital records and property records, as well as other commercially available databases. Federal and state governments and the private sector have widely endorsed EAIV as effective and reliable. *See* PM USA and USSTC January 19, 2012 Comments on Docket No. FDA-2011-N-0467 ("Non-Face-to-Face Sales and Distribution of Tobacco Products and Advertising Promotion, and Marketing of Tobacco Products"), at 4 & nn. 16-18. Congress also endorsed EAIV in legislation that requires those who sell tobacco products in non-face-to-face transactions to use that technology to confirm that the consumer is of legal age to purchase tobacco products. *See* Prevent All Cigarette Trafficking Act of 2009, 15 U.S.C. 376A(b)(4)(A)(iii) (requiring sellers to verify the purchaser's name, birth date, and address through an EAIV database prior to accepting a delivery sale order). Congress recognized the

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Section XI. FDA Should Permit Manufacturers to Describe E-Vapor and Other Noncombustible Products as "Smokeless"

The FSPTCA permits companies to use terms like "smokeless tobacco" and "smoke-free" to describe smokeless tobacco products.[185] FDA should exercise its enforcement discretion to apply this same approach to the deemed, noncombustible tobacco products such as e-vapor and oral tobacco-derived nicotine products that do not contain tobacco. Like smokeless tobacco, these products do not produce smoke, are not combustible, and do not burn. Allowing companies to describe e-vapor and oral tobacco products as "smokeless" and "smoke-free" would be accurate and help consumers understand and distinguish among different tobacco products.

Applying the current requirements of Section 911 to effectively ban describing these products as "smokeless" or "smoke-free" would not survive First Amendment scrutiny because it would serve no legitimate government purpose.[186] "[S]o long as the sale and use of tobacco is lawful for adults, the tobacco industry has a protected interest in communicating information about its products and adult consumers have an interest in receiving that information."[187] Here, manufacturers have a protected interest in conveying the accurate information that products like e-vapor and oral tobacco products do not involve smoke.

FDA could require an appropriate disclosure if it is concerned that some consumers might read a modified risk claim into factually accurate terms like "smokeless" or "smoke-free." For instance, FDA could require a disclosure that such terms are not intended to communicate that a product is reduced risk compared with any other tobacco product. Courts have expressed a clear preference for the use of disclaimers over the suppression of protected speech.[188] The approach

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relevance and importance of age verification procedures in the FSPTCA – it requires FDA to promulgate regulations concerning the sale of tobacco products through means other than face-to-face transactions to prevent sales to minors "including requirements for age verification." *See* January 19, 2012 Comments, at 4 n.16.

[185] *See* FSPTCA § 911(b)(2)(C). Specifically, § 911(b)(2)(C) provides that no smokeless tobacco product will be considered as "sold or distributed for use to reduce harm or the risk of tobacco-related disease" solely because its label, labeling, or advertising uses the following phrases to describe such product and its use: 'smokeless tobacco', 'smokeless tobacco product', 'not consumed by smoking', 'does not produce smoke', 'smokefree', 'smoke-free', 'without smoke', 'no smoke', or 'not smoke'."

[186] *See Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980) (for regulation burdening commercial speech to survive, the government must affirmatively prove that (1) its asserted interest is substantial, (2) the restriction directly and materially advances that interest, and (3) the restriction is narrowly tailored).

[187] *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 571 (2001).

[188] *See, e.g., Zauderer v. Office of Disciplinary Counsel of Supreme Ct. of Ohio*, 471 U.S. 626, 641 n.9 (1985) (the mere possibility that advertising will mislead cannot justify suppression, especially when warning may suffice). *See also Peel v. Attorney Registration and Disciplinary Comm'n of Ill.*, 496 U.S. 91, 111 (1990) (Marshall, J., concurring) (Government may not "ban *potentially* misleading speech if narrower limitations could be crafted to ensure that information is presented in a nonmisleading manner."); *John Doe No. 1 v. Reed*, 561 U.S. 186, 196 (2010) ("Disclosure requirements may burden the ability to speak, but they do not prevent anyone from speaking.") (alterations and internal quotation marks omitted). If the government disfavors certain speech, "the remedy to be applied is more speech, not enforced silence." *United States v. Alvarez*, 132 S. Ct. 2537, 2550 (2012) (quoting *Whitney v. California*, 274 U.S. 357, 377 (1927) (Brandeis, J., concurring)); *see also Sorrell v. IMS Health Inc.*, 131

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that FDA has apparently endorsed for Natural American Spirit cigarettes is instructive. These cigarettes are marketed as containing "100% additive-free natural tobacco" and are accompanied by a disclaimer stating that "No additives in our tobacco does NOT mean a safer cigarette."[189] To date, FDA has not issued any publicly available regulatory action with respect to these statements.

Section XII. FDA Should Not Interpret the FSPTCA's Descriptor Prohibition to Categorically Ban the Use of Words Identified in Section 911 for Deemed TDNPs

In its Preamble to the Proposed Rule, FDA stated that "products deemed under [the final] rule will be subject to the same FD&C Act provisions that cigarettes...are subject to, with respect to the...prohibition against use of modified risk descriptors 'light', 'mild', or 'low' or similar descriptors."[190] This statement suggests that FDA may reflexively apply this prohibition to all deemed TDNPs, without assessing whether such words convey a "modified risk" claim for products other than cigarettes, and with no procedure to make a determination in particular cases.

Although Congress determined that certain words constitute a modified risk claim with respect to cigarettes, it made no such determination with respect to TDNPs, including e-vapor products. FDA should not assume that such words have a similar meaning in this context. If FDA is concerned about the use of specific statutory terms in the labeling, advertising, or brand names of such products, it must create a regulatory process to determine whether the terms actually convey a modified risk claim before categorically barring their use for a particular tobacco product.[191] A blanket extension of the descriptor ban would be contrary to the FSPTCA, the APA, and the Constitution.

The statutory text and history of the FSPTCA do not support a categorical ban on particular terms, like those identified in Section 911, to TDNPs. Section 911 prohibits such terms *only* when they are used as a "descriptor" of "modified risk."[192] Where the terms do not communicate

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S. Ct. 2653, 2671 (2011) ("Vermont may be displeased that detailers who use prescriber-identifying information are effective in promoting brand-name drugs. The State can express that view through its own speech").

[189] *See* https://www.nascigs.com/modules/Security/Login.aspx.

[190] 79 Fed. Reg. at 23143.

[191] John Middleton Co. ("Middleton"), also a subsidiary of Altria Group, Inc., made a separate submission that addresses the extension of the descriptor ban to newly deemed cigars and pipe tobacco. We agree with the points made in Middleton's submission regarding the descriptor ban and incorporate Middleton's comments here by reference. *See* John Middleton Co. Comments on Docket No. FDA-2014-N-0189 (RIN 0910-AG38) (79 Fed. Reg. 23142) (April 25, 2014) – Comments on Proposed Rule "Deeming Tobacco Products Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and FSPTCA; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products" (Aug. 8, 2014). (Descriptor Ban Comments on behalf of John Middleton Co.)

[192] FSPTCA § 911(a), (b). A manufacturer or manufacturers of non-combustible, tobacco-derived nicotine products might at some point apply for and obtain FDA approval of a modified risk claim. But the approval process is onerous. To require a manufacturer to follow that pathway in order to justify the use of words that do not, and are

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anything about risk, Section 911 does not prohibit their use. The legislative context of the provision confirms this reading. The statutory findings about modified risk descriptors focused on only the historical marketing of low-tar cigarettes. The legislative history likewise reflects no Congressional concern about the use of modified risk descriptors for TDNPs, which were not widely available when the legislation was drafted. Were there any doubt that the FSPTCA does not categorically ban specific terms, such as "mild," for these products, the canon of constitutional avoidance – here, avoidance of free speech problems – would resolve the issue against such a ban.[193]

It would be arbitrary and capricious under the APA for FDA to categorically extend the ban on the terms listed in Section 911 to TDNPs without evidence that the terms in fact communicate a modified risk claim.[194] FDA does not cite any scientific evidence to support the proposition that certain terms, when used in the context of TDNPs, convey "unproven modified risk claims" leading to "unsubstantiated beliefs" about the relative risks of such products. Nor does FDA cite any evidence that presumed consumer beliefs about tar and nicotine descriptors in cigarettes influence or predict consumers' understanding of those terms with respect to TDNPs. It would also violate the First Amendment for FDA to extend to TDNPs, the *per se ban* of descriptors tied to cigarettes, without regard to whether the words actually convey any reduced health risk for these other products. The First Amendment protects trademarks, brand designs, labeling, and advertising owned by manufacturers.[195] The Supreme Court has recognized a First Amendment right to communicate with consumers through labeling and advertisements.[196] FDA must show that banning such commercial speech would directly serve a substantial government interest and that less restrictive alternatives are not suitable.[197] To impose a *per se* prohibition on particular terms without a scientific basis for doing so would fail this test.

Absent evidence that the terms included in Section 911in fact communicate a modified risk for TDNPs, FDA at a minimum should make clear that the Proposed Rule does not forbid use of these terms in connection with the marketing, distribution and sale of those products.

In addition, the Agency should adopt a procedure to assess whether terms used with regard to a particular product are, when considered in context, "descriptors" of "modified risk," or conversely, whether those terms convey no health risk-related information.[198] Such an evidence-based procedure would adequately protect the government's interest in preventing the use of certain words as descriptors of modified risk. It would allow FDA to make an informed

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not intended to, communicate a health claim, would serve to ban those words at least during the period – potentially years – required for the manufacturer to develop and FDA to consider the application.

[193] *See also supra* pp. 37-38 (discussing constitutional avoidance doctrine).

[194] *See also supra* p. 37 (discussing the relevant standard under the APA).

[195] *Hurley v. Irish-Am. Gay, Lesbian and Bisexual Group of Boston*, 515 U.S. 557, 569-70 (1995).

[196] *See, e.g., Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 647-48 (1985) (use of illustrations or pictures in advertisements serves important communicative functions); *Friedman v. Rogers*, 440 U.S. 1, 11 (1979) (trade name is commercial speech); *Piazza's Seafood World, LLC v. Odom*, 448 F.3d 744, 753 (5th Cir. 2006) (First Amendment protects trade name).

[197] *See also supra* p. 43 (discussing the relevant First Amendment standard established by *Central Hudson*).

[198] *See* FSPTCA § 903(b).

evaluation of the issue in the context of a particular tobacco product and specific uses of the terms. Without such a process, FDA's rule would unnecessarily and unjustifiably restrict manufacturers' protected speech in violation of the First Amendment.

Section XIII. Any Action FDA Takes with Regard to Flavored Noncombustible Tobacco Products Must Be Science-and Evidence-Based, Should Respect Adult Tobacco Consumer Preferences and Consider the Positive Role that Flavors May Play in Harm Reduction

The Preamble to the Proposed Rule states that "FDA is aware that some tobacco products, such as e-cigarettes and certain cigars, are being marketed with characterizing flavors, and that these flavors can be especially attractive to youth."[199] FDA further states that "many of the products proposed to be covered by this rule are offered in fruit and candy flavors, such as chocolate and grape flavors, making them especially attractive to children and young adults."[200] FDA requests comments on what, if any, additional actions it should take "to address the sale of candy and/or fruit flavored products to children and young adults," and specifically states that FDA may establish a product standard "prohibiting flavors" in deemed products.[201]

When considering any additional actions to regulate the marketing of deemed tobacco products with characterizing flavors, we offer several guiding principles, including the following:

- Kids should not use any tobacco products, with or without characterizing flavors, and the FSPTCA provides FDA with ample tools to combat the use of tobacco products by minors.
- Tobacco product manufacturers should not use children's cartoons or youth-oriented candy trademarks.
- Any action FDA might take regarding currently marketed, deemed tobacco products with characterizing flavors must follow the process that Congress established in Section 907 of the FSPTCA and should be science- and evidence-based.
- Clear definitions are necessary for a science- and evidence-based determination regarding whether any restrictions on tobacco products with certain characterizing flavors are appropriate for the protection of the public health.

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[199] 79 Fed. Reg. at 23144.

[200] 79 Fed. Reg. at 23146. Throughout the preamble, FDA uses inconsistent, undefined terms when discussing the use of flavors in tobacco products. For example, FDA refers to products "marketed with characterizing flavors" (79 Fed. Reg. 23114); "flavored tobacco product usage" (*Id.*); "fruit and candy-flavored e-cigarette liquid," (*Id.*); "flavorants" in new tobacco product applications (79 Fed. Reg. 23147); and establishing a product standard "prohibiting flavors." (*Id.*). These disparate references make it difficult to respond to the precise issues under consideration by FDA and highlight the need for clear definitions. For present purposes, we use the term "characterizing flavor" while commenting on the potential regulation of e-vapor and other noncombustible, newly deemed tobacco products that have an identifiable and predominant flavor other than tobacco.

[201] 79 Fed. Reg. at 23147.

- FDA should take adult consumer preferences into account if and when it considers product standards relating to characterizing flavors.

Kids should not use any tobacco product and access to tobacco products, including those with characterizing flavors, should be strictly limited to adults. As noted in Section VIII, we support FDA's Proposed Rule to establish a minimum age of 18 to purchase any tobacco product. In addition, the FSPTCA provides FDA with other tools to combat the use of tobacco products with characterizing flavors by minors. For example, when FDA finalizes the Proposed Rule, it can inspect retail stores to ensure that they conduct appropriate age verification.

Many have expressed anger and frustration at certain tobacco product manufacturers using children's cartoon characters and youth-oriented candy trademarks to market their products. Nu Mark does not market in this way, and shares the concern. No tobacco product manufacturer should use names such as Poppa Smurf, Curious George,[202] Sweet Tarts, and Skittles[203] to market their tobacco products. We believe addressing such activities should be part of FDA's initial focus as it regulates deemed tobacco products. For example, FDA could work with the legitimate owners to enforce their intellectual property rights against infringing entities inappropriately using their children's cartoon characters or trademarks associated with youth–oriented products.

If and when FDA takes action to regulate deemed tobacco products with characterizing flavors, it must follow the process Congress established in Section 907.[204] This approach would ensure that any proposed regulatory action is supported by science and evidence, that the public is provided with notice and an adequate opportunity to comment, and that any standard is uniformly applied to all regulated entities.

In addition, FDA must consider unintended consequences and other countervailing effects associated with a proposed product standard before promulgating a final regulation.[205] For example, in the context of e-vapor products, FDA would need to consider whether a ban on products with a defined characterizing flavor could result in demand for contraband products having that flavor, including liquid flavors or other items consumers use to vape. Contraband products would not be subject to FDA regulatory oversight and the important public health requirements of the FSPTCA.

FDA should be mindful of the difficulty in defining and identifying "characterizing flavors." Clear definitions and methodologies are necessary for science- and evidence-based determinations regarding whether restrictions on a particular characterizing flavor for a defined tobacco product category are appropriate for the protection of the public health. We are not

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[202] *See, e.g.*, http://www.bmorevapes.com/The-Poppa-Smurf-E-Liquid_p_73.html (accessed on June 13, 2014); http://www.fluidvaper.com/curiousgeorge.

[203] *See, e.g.*, http://www.volcanoecigs.com/sweet-tart-eliquid-15ml.html (accessed on June 13, 2014); http://vaporsniper.com/premium-e-liquids/vapor-sniper-vapor-liquid/skittles-smoke-juice-eliquid-ejuice-vapor-liquid-sniped.html.

[204] Of course, any product standard that restricts the use of ingredients in noncombustible tobacco-derived nicotine products, and other newly deemed tobacco products, must likewise adhere to the requirements of Section 907.

[205] FSPTCA § 907(b)(2).

aware of any standardized method for determining what constitutes a tobacco product with a "characterizing flavor."

The ambiguity of defining tobacco products with characterizing flavors is evident in various published surveys. For example, the Legacy Young Adult Cohort study asks respondents to identify the tobacco product brands used in the past 30 days and whether the products are "candy-, fruit-, or alcoholic-beverage flavored."[206] The National Adult Tobacco Survey asks respondents whether tobacco products they used were "flavored to taste like candy, fruit, chocolate, or other sweets."[207] Other surveys use less specific questions to measure use of flavored tobacco products. For example, the Canadian Youth Smoking Survey asks if respondents have used "flavored little cigars" and the 2011 NYTS[208] asks a similar non-specific question.[209]

Congress intended for FDA to respect ATCs' preferences and FDA should take these preferences into account when considering any product standard. A stated purpose of the FSPTCA is "to continue to permit the sale of tobacco products to adults in conjunction with measures to ensure that they are not sold or accessible to underage purchasers."[210]

E-cigarettes are primarily used by ATCs looking for an alternative to combustible cigarettes.[211] Evidence related to the importance of flavors to adult e-cigarette consumers, however, is limited to date.[212] Dawkins *et al.* found that approximately 90% of adult e-cigarette consumers report using flavored products.[213] Farsalinos *et al.* asked 4,618 e-cigarette consumers about the type of flavors they used regularly, whether the variety of flavorings was important in reducing or completely switching from smoking, and their reasons for using multiple flavors.[214] Findings included the following:

- Most e-cigarette consumers use three different types of flavors on a regular basis.
- On a scale of 1 to 5, e-cigarette consumers reported variability of flavors was "very important" (score = 4) in their effort to reduce or quit smoking.
- The most commonly used flavors were fruits, followed by sweets and tobacco.
- The majority of participants said that restricting variability of flavors would make the e-cigarette experience less enjoyable.

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[206] Villanti *et al.* (2013).

[207] King *et al.* (2013).

[208] Note that the 2012 NYTS survey instrument was modified to include the following question: "Were any of the tobacco products you used in the past 30 days flavored to taste like menthol (mint), clove, spice, alcohol (wine, cognac), candy, fruit, chocolate, or other sweets?"

[209] King *et al.* (2014); Leatherdale *et al.* (2011).

[210] FSPTCA § 3(7).

[211] *See* Section IV, *infra*.

[212] As with FDA's preamble discussed above, different studies use different and/or undefined terms when talking about the use of flavors in tobacco products.

[213] Dawkins *et al.* (2013).

[214] Farsalinos *et al.* (2013).

- Almost half of study participants said that a lack of a variety of flavors would increase craving for tobacco cigarettes and would make reducing or completely switching from smoking less likely.
- Regression analysis showed that the number of flavors regularly used was associated with smoking abstinence.

Farsalinos *et al.* concluded: "The results of this survey indicate that [e-cigarette] liquid flavourings play a major role in the overall experience of dedicated consumers and support the hypothesis that they are important contributors in reducing or eliminating smoking consumption."

Evidence related to the role of flavors in e-cigarette use patterns among youth is also limited. A 2013 study by Pepper *et al.* involving a national U.S. sample of 228 males ages 11-19 explored awareness of and willingness to try e-cigarettes.[215] The majority (67 %) of study participants had heard of e-cigarettes, < 1% (only 2 participants) had ever tried an e-cigarette. Eighteen percent of participants reported a willingness to try an e-cigarette if offered one by a friend, but there was no difference based on whether the e-cigarette was flavored.[216] The strongest predictor of willingness to try an e-cigarette was whether the participant was a smoker of conventional cigarettes.[217] The researchers concluded: "This preliminary finding suggests that, at present, candy or fruit flavors do not increase the attractiveness of e cigarettes to adolescents."

For ATCs, these studies suggest that characterizing flavors could play a role in facilitating trial and possible adoption of e-cigarettes. As we explain in Section IV, the use of noncombustible tobacco products, such as e-cigarettes, likely pose a far lower health risk to individual consumers when compared with combustible tobacco products. Evidence also suggests that noncombustible products may facilitate complete switching from conventional combustible tobacco products. In the study about youth use patterns, findings suggested that flavors were not a significant motivating factor in adolescents' interest in trying e-cigarettes. With limited studies to date, however, additional research in these areas is needed.

Section XIV. Manufacturers or Importers Should Be Able to Assign Responsibilities for Submitting Information or Filing Applications

In some instances, the company distributing a particular product is not the manufacturer of that product. For example, Nu Mark has a third party manufacture its e-vapor products. For these situations, FDA should make clear in the preamble to the Proposed Rule, or in guidance, that it will permit manufacturers or importers to assign by written contract their responsibilities under the FSPTCA for submitting information or filing applications.

The Proposed Rule would impose a number of requirements on manufacturers or importers of the tobacco products. It would require that they

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[215] Pepper *et al.* (2013).

[216] Of the 18% reporting a willingness to try an e-cigarette, 13% were willing to try an e-cigarette without flavors, and 5% were willing to try either a flavored or unflavored e-cigarette or both.

[217] This particular finding aligns with the conclusions of other studies discussed in Section IV, *supra.*

- submit certain health information to FDA pursuant to Section 904;
- register and list products pursuant to Section 905;
- provide product information and submit substantial equivalence reports prior to the introduction of certain new tobacco products pursuant to Section 905;
- report the removal of tobacco products from the market and fulfill related recordkeeping obligations pursuant to Section 909; and
- file a premarket review application pursuant to Section 910.

In a situation where tobacco products are manufactured overseas and imported into the United States by one or more companies, and then sold to another company that holds the distribution and/or marketing rights within the United States, it may be more efficient to allow this secondary seller to undertake some of the requirements otherwise imposed on the manufacturer or importer. This is particularly so where the entity also develops the specifications for the product, contracts for its manufacture, has rights to intellectual property in connection with the product or its branding and/or maintains confidential formula or other such information on inputs to the tobacco product.

There is nothing in the FSPTCA that would prohibit such an assignment. In fact, there are provisions in the FSPTCA that allow a third party to act on behalf of a manufacturer or importer. Section 904 permits an agent to submit health information on behalf of a manufacturer or importer. In addition, FDA has issued guidance providing that "[a]n owner or operator may authorize a third party agent to register and submit product listing information on its behalf."[218] In other contexts, FDA permits entities in the supply chain to assign certain regulatory responsibilities and obligations to third parties. For example, FDA's clinical research regulations permit a clinical trial sponsor to assign its obligations for managing a clinical trial to a contract research organization ("CRO").[219] FDA's over-the-counter ("OTC") drug regulations also allow "private label distributors,"[220] whose name and brand appear on the product label, to assign adverse event reporting obligations to the product manufacturer or other third parties.[221]

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[218] FDA Guidance for Industry, Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments (Revised April 2014).

[219] *See* 21 CFR § 312.52 ("A [clinical trial] sponsor may transfer responsibility for any or all of [its] obligations . . . to a contract research organization. Any such transfer shall be described in writing. If not all obligations are transferred, the writing is required to describe each of the obligations being assumed by the contract research organization. If all obligations are transferred, a general statement that all obligations have been transferred is acceptable. Any obligation not covered by the written description shall be deemed not to have been transferred.").

[220] Private-label distributors are entities - typically retailers - who purchase pre-formulated goods from third-party manufacturers, but distribute the finished product under their brand or trade names. In most cases, the private-label distributors receive and handle customer inquiries and complaints for the products they distribute, but they may assign to the product manufacturer the responsibility for evaluating such complaints for purposes of complying with adverse event reporting requirements.

[221] *See* FDCA § 760 (b)(2) ("A retailer whose name appears on the label . . . as a distributor may, by agreement, authorize the manufacturer or packer of the nonprescription drug to submit the required [adverse event] reports for such drugs to the [FDA] so long as the retailer directs to the manufacturer or packer all adverse events associated with such drug that are reported to the retailer . . . .").

Allowing a manufacturer or importer to assign its regulatory responsibilities to a third party can provide greater efficiency and help ensure accurate and timely compliance. A third party such as the second seller described above may be more likely to possess the information necessary to make the filings required under the FSPTCA and may be the only entity in the supply chain that possesses complete information. The FSPTCA filing requirements currently are imposed on either the manufacturer *or* importer, and FDA allows the companies to decide which entity will be responsible. We request that FDA clarify that such assignments are not prohibited so that the key entities involved in the design, research, scientific testing and assessment, manufacture, introduction into domestic commerce and commercial marketing of tobacco products have the flexibility to determine among themselves the best candidate for complying with filing requirements.

In addition, an entity that contracts for the manufacture of the product and has the distribution rights to such product in the United States will have greater financial and reputational incentives to address any issue with FDA. FDA may find it less burdensome to engage with the entity having ultimate responsibility for the domestic sale of the product rather than a foreign manufacturer or importer.

Section XV. Meaningful Testing for Harmful and Potentially Harmful Constituents Will Require a Category Specific List of Constituents, Testing Protocols, Validated Consensus Standards and Certified Reference Products

When the Proposed Rule becomes final, deemed products, including e-vapor products, will be subject to the same general FSPTCA provisions as cigarettes and smokeless tobacco, including reporting of harmful and potentially harmful constituents ("HPHCs").[222] Nu Mark supports HPHC testing and reporting requirements for e-vapor and other TDNPs. However, in order to produce data useful for product comparisons or other decision-making, FDA will need to develop category-specific HPHC lists; establish protocols and validated consensus standards; utilize certified reference materials to ensure the integrity of the data FDA seeks; and implement laboratory proficiency testing.

In meeting Section 904 requirements for currently regulated tobacco products such as cigarettes, smokeless and roll-your-own tobacco, FDA had the benefit of decades of manufacturers' and contract laboratories' experience testing constituents.[223] This is not the case for TDNPs, such as e-vapor products, because testing protocols and validated consensus standards are nonexistent.

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[222] 79 Fed. Reg. at 23143. Section 904(a)(3) of the Tobacco Control At provides "Each tobacco product manufacturer or importer, or agents thereof, shall submit to the Secretary the following information....a list of all constituents, including smoke constituents as applicable, identified by the Secretary as harmful or potentially harmful to health in each tobacco product, and as applicable in the smoke of each tobacco product, by brand and by quantity in each brand and subbrand."

[223] *See* Letter from James E. Dillard III to Division of Dockets Management re: FDA-2011-N-0271 – Request for Comments on "Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke," October 11, 2011; Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2012-D-0049 – Comments on Draft Guidance Entitled "Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under the Federal Food, Drug, and Cosmetic Act," June 1, 2012; Letter from James

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To ensure that HPHC testing and reporting requirements are appropriate, FDA should develop e-vapor and other category-specific HPHC lists as it did for cigarettes, smokeless tobacco, and roll-your-own testing and reporting requirements.[224] FDA should also gather additional evidence regarding tobacco-derivatives other than nicotine that may be added by some manufacturers. FDA should begin this work by defining the purpose of the HPHC lists. That purpose should be specific enough to allow scientifically-informed decision making.

Protocols and validated consensus standards must be developed. No formal protocols exist today for measuring constituents in e-vapor products[225] or oral TDNPs. In the absence of standardized protocols, constituent testing and reporting will be of limited utility. For example, independently developed and implemented analytical methods according to manufacturers' or laboratories' internal processes will result in significant changes over time and statistically significant lab-to-lab differences for many constituents, limiting reproducibility and comparison across labs.

Organizations like the Cooperation Centre for Scientific Research Relative to Tobacco ("CORESTA") are attempting to standardize testing protocols for e-vapor products.[226] We encourage FDA to engage with CORESTA as that organization continues its work in this area. In addition, voluntary consensus standards for constituent testing are needed.[227] The absence of voluntary consensus standards means HPHC data will be inconsistent and unreliable for product comparisons and other decision making. While a handful of voluntary consensus standards exist for cigarettes, smokeless and roll-your-own tobacco, none exist today for e-vapor products or other oral tobacco-derived nicotine products. Both FDA and manufacturers will waste resources and time testing for constituents for which there are no validated, standardized methods and little evidence of either presence or biological relevance of the constituent.

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E. Dillard III to Office of Information and Regulatory Affairs re: Docket No. FDA-2012-D-0049/0MB Control Number 0910-NEW (77 Fed. Reg. 44636) (July 30, 2012)-Comments on "Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under the Federal Food, Drug and Cosmetic Act," (August 29, 2012); Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2012-N-0212 - Comments on the Tobacco Product Analysis Scientific Workshop (September 30, 2013).

[224] For example, FDA's abbreviated list of HPHCs requires manufacturers or importers to provide quantitative information for nine constituents for smokeless tobacco, 18 constituents for cigarettes and six constituents for cigarette filler and roll-your-own tobacco. *Draft Guidance for Industry Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug and Cosmetic Act* (March 2012), *available at* http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM297828.pdf.

[225] *See* Orr (2014) ("Currently, standardised testing paradigms for the e-liquid and e-cigarette aerosols have not been determined. The development of a scientific consensus on the most appropriate testing paradigms to be used for comparative analyses of e-cigarette products is critical."); Cheng, T., "Chemical evaluation of electronic cigarettes," Tob Control 2014; 23:ii11-ii17 (February 2014) ("[I]t would be helpful to develop validated analytical test methods to measure chemicals of interest in e-cigarettes.")

[226] www.coresta.org, Study Groups, Product Technology.

[227] See ALCS submission "Comments on Draft Guidance Entitled "Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and tobacco Smoke Under the Federal Food, Drug and Cosmetic Act" (June 1, 2013) which states that for cigarette smoke testing under the ISO smoking conditions, 14 of the 18 constituents on the abbreviated HPHC List have standardized methods developed through a Voluntary Consensus Standard process. There are no standardized methods for the Canadian Intense smoking condition. For tobacco (both smokeless and tobacco used in cigarettes), it is only three out of ten.

No certified reference products exist for e-vapor products or other TDNPs. Certified reference products will play an integral role in comparing analytical results from different laboratories at a single point in time as well as across laboratories over time.[228] Certified reference products would also help facilitate the establishment of validated HPHC analytical methods in laboratories and in conducting performance evaluations of laboratories.

We encourage FDA to establish a certification process for reference products. FDA's recent efforts to create certified reference products for cigarettes provide a useful model for how the Agency could develop reference products for e-vapor products and other TDNPs.[229]

Laboratory proficiency testing should also be part of the HPHC testing and reporting process. Such testing provides assurance that the quality of the data is comparable to reference values or to the performance of similar laboratories. Results from proficiency testing can provide FDA confidence in data and insight into inter-lab differences. Proficiency testing results will help increase the understanding of the effectiveness, comparability and performance characteristics of method(s). These results will also create the potential to assign values to reference products and offer an opportunity to evaluate new sample matrices.

FDA should develop category-specific HPHC lists; establish protocols and validated consensus standards; utilize certified reference materials to ensure the integrity of the data FDA seeks; and implement laboratory proficiency testing prior to requiring HPHC reporting.

Section XVI. Conclusion

The potential for TDNPs, such as e-vapor products, to offer reduced risk product options for ATCs is already evident. The combination of new, innovative, and potentially less harmful tobacco products and ATC interest in them presents FDA with an unprecedented opportunity to reduce the harm associated with tobacco use. We support FDA extending its regulatory authority over all tobacco products and urge FDA to implement flexible, reasonable and thoughtful regulation that can spur innovation in e-vapor and other TDNPs. As it does so, we hope FDA will consider these comments in developing any Final Rule and determining how to apply the FSPTCA's provisions to deemed products.

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[228] ISO GUIDE 30:1992(E)/Amd.1:2008 defines certified reference materials as "reference material characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability."

[229] *See* CTP Awards Cooperative Agreement to Develop a Cigarette Tobacco Reference Products Program to University of Kentucky, *available at* http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/AbouttheCenterforTobaccoProducts/ucm391336.htm.